DISEASES *of the* CHEST

VOLUME XV, JUNE, 1949 NUMBER 6

The Value of Streptomycin in the Treatment of Tuberculosis*

HENRY C. SWEANY, M.D., F.C.C.P.
Chicago, Illinois

It is with the greatest pleasure that I accept the invitation to deliver an address dedicated to the memory of Dr. Carl A. Hedbloom. I do this with great humility and almost a feeling of inferiority. We all recognized the worth of Dr. Hedbloom while he was in our midst, yet as the years have passed his greatness has become even more magnified. Without detracting from the merit of the fine young surgeons of the present time, I believe I may say that he stands alone among the chest surgeons of Chicago, having established in his specialty a tradition that will go down in medical history and will always be an inspiration for others to follow.

Owing to the broad scope of the subject, the discussion of "The Value of Streptomycin in the Treatment of Tuberculosis" must be a general one, including references to the work already done as well as to our own incompleted studies. Rarely has any medical problem expanded so rapidly, so extensively and so successfully. Within a period of five years, Streptomycin has made more progress in the therapy of tuberculosis than all the other drugs of the past. Before the advent of Streptomycin, hundreds of serums, vaccines and chemicals of all sorts had been tried with little or no success. The results were generally so discouraging that there

*The Hedbloom Lecture, given February 16, 1949, before the faculty and students of the University of Illinois College of Medicine under the auspices of Phi Beta Pi Medical Fraternity.

From the Laboratories of the City of Chicago Municipal Tuberculosis Sanitarium.

This investigation was supported (in part) by research grants from the Division of Research Grants and Fellowships of the National Institutes of Health, U. S. Public Health Service.

was faint hope a therapeutic remedy would ever be found for tuberculosis.

Domagk's[1] discovery of sulfa, however, opened a new line of search for chemotherapeutic remedies. Thousands of sulfa compounds were prepared not only for use against acute infections but for experimental study in the treatment of tuberculosis. Although a few sulfones were hailed with considerable enthusiasm, so far as tuberculosis was concerned little gain was achieved.

It was Fleming's[2] work on Penicillin, however, that began a new era in drug therapy and led to the present enviable position held by antibiotic therapy.

The Discovery of and Early Experiments with Streptomycin

The discovery of Streptomycin was almost as phenomenal as that of Penicillin. Waksman[3] observed that practically no other micro-organisms were present in soil where certain Streptomyces existed. By growing some of these Streptomyces in media he was able to extract a substance that would suppress the growth of many bacteria. This product was called "Streptomycin," and Schatz, Bugie and Waksman[4] first showed the anti-bacterial effect of an extract of the *Streptomyces griseus* on bacterial cultures. Four grams of the "Streptomycin" were prepared for Feldman and Hinshaw[5] and later Feldman, Hinshaw and Mann[6] of the Mayo Clinic to try out on experimental tuberculosis in guinea pigs. The results were so encouraging that the immediate preparation of the product by the Merck Company was begun. As soon as the first product was ready it was tried out in pulmonary tuberculosis by Hinshaw and Feldman[7] and others at the Mayo Clinic.[8-14]

Their work was a fair index of all that followed, and their conclusions were generally correct. They first showed that pulmonary tuberculosis could be considerably suppressed by the use of Streptomycin; that acute disease responded more readily than chronic disease; that cases of genito-urinary tuberculosis made a remarkable improvement after treatment with streptomycin, but that many relapses occurred. The drug was found to be useful in the treatment of tuberculous sinuses, tuberculous laryngitis and tuberculous tracheo-bronchitis; certain forms of miliary tuberculosis responded well. Even the dreaded tuberculous meningitis could be affected so that the lives of the patients were prolonged and some patients apparently cured of the disease.

It was soon obvious, however, that something was lacking; certain cases after a temporary improvement reversed their favorable course and became worse. As was soon discovered by Youmans, Williston, Feldman and Hinshaw[15] this was largely due to the

development of resistance to the drug by the tubercle bacillus. This resistance proved to be "the only discordant note in an otherwise perfect symphony."

The first experiments conducted at the Mayo Clinic created an air of expectancy in the medical world and caused those interested in tuberculosis to turn their attention to the use of this promising antibiotic.

The Work in the Veterans' Administration, The Army and The Navy

The Veterans' Administration, the Army and the Navy combined their efforts in one of the most elaborate experiments ever conducted in medicine. Protocols were laid down for the selection of cases, the time of treatment and the follow-up after completion of treatment. About two times each year a joint conference was held and all the data was assembled and discussed. Progress reports have appeared from time to time in medical journals.

Two of the first significant reports were published by McDermott, Munschenheim, Hadley, Bunn and Gorham[16a] and by Munschenheim, McDermott, Hadley, Hull-Smith and Tracy.[16b] These authors listed three cardinal features of the results of Streptomycin treatment, viz: (a) a rapid, sometimes abrupt, fall in temperature and accompanying symptomatic improvement not unlike the crises observed in pneumococcus pneumonia; (b) a regression and frequently a complete disappearance of the pulmonary lesions demonstrable roentgenologically and (c) the development of strains of tubercle bacilli which were resistant to the action of streptomycin in vitro.

The earliest comprehensive report of the whole study appeared in December 1947, under the authorship of Barnwell, Bunn and Walker.[17] The criteria laid down for the selection of cases was rigid, namely: there must be in each case selected a proved diagnosis, a minimal or moderately advanced exudative type of lesion or, if far-advanced, a prognosis of at least one year without Streptomycin. The patient must have been observed for 60 days and must not have shown any regressive changes during that period of time. Recent spreads or pneumonias were accepted. The same regimen was to be followed throughout the course of the drug treatment, for example: a patient receiving pneumothorax was to be continued on pneumothorax as before; no surgical procedure was to be instituted during the course of the Streptomycin treatment, and an observation period of 120 days was outlined for each patient. The age limit for acceptable cases was 45 years.

Complete urine examinations were required three times before the beginning of treatment and every two days thereafter. Urea

clearance tests, non-protein nitrogen of the blood, sedimentation rates and sputum analyses were performed regularly. X-ray films were taken before the treatment and every two weeks after the treatment was begun. The pulse, temperature and weight were regularly recorded.

The dosage selected was the same as that used in the latter part of the work at the Mayo Clinic, namely, 1.8 gms. a day, given in six equally divided doses, for a period of 120 days. The development of ear damage was controlled by caloric tests and audiograms before the treatment, at weekly intervals during treatment and at the end of the treatment.

Analysis of these cases was carried on in a unique manner. The President of the American Trudeau Society was called upon to appoint a jury of seven experts to read the roentgenograms. The x-ray films were read individually by these men without any of them knowing whether a patient had or had not been treated; nor did any member of the jury know what the others had reported with regard to any film. In spite of the fact that two-thirds of the lesions had showed progression before treatment was begun and that, according to the jury, 58 per cent would probably not have changed for the better if left on bed rest alone, 85 per cent of the "exudative" lung lesions showed some clearing.

In general, the reduction of subjective clinical symptoms was quite dramatic. Every patient on Streptomycin developed rather abruptly a feeling of well being. The appetite improved in 85.2 per cent of the treated cases; weight increased in 84.3 per cent; cough decreased in 79.8 per cent; sputum decreased in 79.8 per cent; temperature decreased in 73.1 per cent; sedimentation rate decreased in 51.1 per cent, and sputum conversions were reported in 43 per cent during the treatment.

The authors reported, however, that little or no substantial improvement occurred in the "proliferative" or "fibro-ulcerative" cases, since the treated and untreated groups remained about the same.

It was noticed that there were certain signs of toxicity that could not be disregarded, especially the damage done to the eighth nerve. There was a vertigo in 92 per cent of the patients treated and an absence or dimunition of caloric stimulation in 77 per cent—indicating a definite injury to the labryrinthine branch of the eighth nerve. There were many other minor variations from the normal: nausea and vomiting in 10 per cent, elevation of temperature in 9 per cent, eosinophilia in 70 per cent, pruritis in 18 per cent, renal casts in 67 per cent, albumin in the urine in 20 per cent, and in 2.3 per cent treatment had to be discontinued because of urinary retention.

The problem of resistance was studied by Youmans and his associates[18] who stated that 14 of 18 cultures (77 per cent) developed resistance in vitro. Wolinsky, Renginster and Steenken[19] found resistance after twelve weeks treatment in 37 per cent of 47 cases.

As a result of the difficulties encountered with drug toxicity, bacillary resistance and various other factors, a much wider scope of study was outlined by the above mentioned Government Services.[20] Several different categories with regard to dosage and length of time of treatment were outlined and followed. As a result of this second report, involving 2,780 cases, the authors were able to state among other things that in addition to the previous findings the one-gram dosage was as satisfactory as the two-gram and that probably even 0.5-gram sufficed. One of the most important observations was that a remarkably small number of complications resulted from the half-gram dose given in two equal daily injections. The one-gram dose produced less than half the number of complications resulting from the administration of the two-gram dose; the half-gram dose produced only a half to a quarter as many complications as the one-gram dose. In fact, of 137 cases treated with the 0.5-gram dose there were no cases in which the caloric stimulation was entirely absent and none in which there was diminished hearing to voice sound, while only 5.8 per cent of the cases revealed vertigo, compared with 23.1 per cent of those on one-gram dosage and 80 per cent on the two-gram dosage.

There was a clinical improvement in practically 75 per cent of all cases treated. The jury (now of ten men) reported that only 9 to 13 per cent of the cases had improved before the drug was given and that 71 to 75 per cent showed improvement roentgenologically after the drug was given. In spite of this favorable showing, the authors warned that every case of tuberculosis was not suitable for treatment and that very few cases cleared completely. Most of the roentgenograms cleared only partially; relapses occurred in 7 to 10 per cent of cases during treatment and 14 to 29 per cent after treatment.

Since that report, the time of treatment has been further reduced to 42 days in an attempt to avoid development of resistance of the bacillus.

By this time they were also able to offer a more favorable appraisal of the treatment of certain complications. The results of the work on bones and joints was particularly gratifying; 40 per cent of the cases improved during treatment and 70 per cent after the termination of treatment, whereas 70 per cent of cases were progressive when treatment was begun. The treatment of

tuberculosis of the genito-urinary tract produced symptomatic improvement, cystoscopic improvement, and a conversion in bacillary content in 80 per cent of the cases treated, while only 15 per cent showed relapses. The only difference between this complication and some of the others was that better results were obtained on the two-gram than on the one-gram dosage. The most disappointing of all the complications treated were the miliary and meningeal lesions. While it was true that many cases made temporary recoveries and that something had been accomplished in the treatment of tuberculous meningitis that had never before been done, nevertheless, only a small percentage of the total number of cases treated ultimately survived. The work from the Service groups was reported recently by Bunn[21] who has followed the cases from the beginning of treatment. Out of 100 such cases only 24 were alive from 11 to 25 months after treatment; of this 24 only 15 were entirely well. A further break-down of the 24 living cases revealed that 12 were of the 22 miliary cases, 9 were of 43 simple meningitis cases and only 3 were of 35 cases of miliary meningitis cases.

Treatment of other complications produced results similar to those reported in the preliminary series. Included were gastrointestinal lesions, laryngeal lesions, lesions of the cutaneous sinuses, of the mouth, the pharynx, and of the tracheobronchial tree and many other complications where there were not a great many cases treated. For example, in tuberculous lymphadenitis, out of 36 cases there were 12 in which the lymph node enlargement had disappeared; in 18, nodes were much smaller and in only six were the findings stationary. There were good results in many cases of tuberculous peritonitis; 19 of 27 cases improved, with some showing complete recovery. In otitis media, 11 out of 13 cases improved and some were healed completely. Several cases of pericarditis were apparently healed. Particularly gratifying were the results from thoracic surgery, especially on pulmonary resection where there was a percentage of only 2.8 per cent postoperative spread, compared with a very much higher percentage before the use of Streptomycin. The results with other types of lung surgery were not especially remarkable.

The authors reiterated that there was little or no effect on chronic fibroid pulmonary tuberculosis. The effect on cavities was unpredictable and if any favorable action was present it was usually temporary. Because of the possibility of the development of resistance, it was recommended that Streptomycin treatment not be used in minimal cases of tuberculosis which could be well handled by other means.

An important observation was that collapse therapy was made

feasible in 20 per cent of their cases as the result of Streptomycin treatment. They recommended that collapse therapy be initiated before resistance of the micro-organism developed.

The Work of the American Trudeau Society and the Tuberculosis Study Section of the U. S. Public Health Service

Almost simultaneous with the program outlined and followed by the Service groups was the work of the American Trudeau Society* in conjunction with the Tuberculosis Study Section of the United States Public Health Service.** In fact, there was an over-lapping of the workers in these two groups; a great many in the Service groups were on the Committee of the United States Public Health Service Study Section. This Committee has met two or three times a year and passed upon appropriations for various hospitals and institutions outside of the Government Services. A large number of separate studies are being supervised by the Committee, which in addition has undertaken a vast experiment in which a large number of cases are being treated with matched controls. It is too early yet to expect an analysis or evaluation of the results of this interesting study.

Like the Service groups, and profiting by their experience, the United States Public Health Service Committee found it necessary to outline several categories for the study of the length of time and dosage. Dosage schedules were reduced from two-grams to a rough "gram per body weight" dosage of 0.75 to 1.5 grams, depending on the weight of the individual. Also, as in the Service groups, the time element was reduced from 120 to 90 and then to 60 days.

Some of these studies have already been published. A representative report is one by Amberson and Stearns[22] which has summarized the situation clearly with regards to indications, complications, dosage, time of treatment and results.

Studies Abroad

As soon as the drug was available, work was begun in many of the countries of Europe and Latin America. Some of the earliest and most important reports, largely concerned with the treatment of generalized tuberculosis, include those of Cocchi and Pasquinucci[23] in Italy; Debré,[24] Decourt,[25] DeLavergne,[26] and Bernard[27] and their respective associates in France; Van Goidsenhoven and his associates[28] in Belgium; Marshall[29] and his many associates in England and Loffler[30] and his many associates in Switzerland. A significant fact observed was that there was

*Dr. McCloud Riggins, President, succeeded by Dr. H. Corwin Hinshaw.
**Dr. E. R. Long, General Chairman, and Dr. H. Stuart Willis, Chairman.

immediate favorable clinical effect in the majority of all treated cases of generalized tuberculosis, resulting in a relief of symptoms and prolongation of life.

They found recurrences of the disease in most of the treated cases, and that apparent recoveries varied from 50 per cent down to around 10 per cent of the cases. This variation depended on several factors, the most important of which was the length of time the cases were followed after treatment. Another important factor was the type of the disease; the mortality was highest in miliary meningitis, lower in simple meningitis and lowest in miliary tuberculosis. In addition, results were reported to be better in proportion to the shortness of the disease's duration before treatment. Finally, patients with meningitis fared better with intrathecal treatment, but it was necessary that the dosage be kept low (between 25 to 50 mgs.) and given at the onset every two to three days and then at various longer intervals. Many of the authors claimed an advantage in the intrathecal use of various ancillary drugs (sulfones, vitamins, etc.) with Streptomycin.

The Streptomycin Work at the Municipal Tuberculosis Sanitarium

About November 1946, the first cases were treated at the Municipal Tuberculosis Sanitarium. At first we were obliged to treat only those patients who were able to buy the drug themselves.

This situation proved to be most unsatisfactory since it resulted in the treatment of many unsuitable cases which not only were left unimproved but also were subject to the ear damage commonly resulting from the large dosage employed at that time. The two-gram dosage was soon supplanted by a modified dosage outlined by the Tuberculosis Study Section of the United States Public Health Service, with a marked reduction in ear complications. A Streptomycin Board* was appointed to study each case carefully and make selections for treatment on the basis of indications already determined, to obtain the maximum results and to prevent drug toxicity as much as possible. About all that could be done under the existing conditions, however, was to watch for signs of toxicity and to classify the cases into those having good and poor indications, since anyone might buy his own drug.

In November 1947, the problem was greatly simplified when the Board of Directors** of the Institution provided for the purchase of Streptomycin for all patients who might benefit from the use

---

*LeRoy Berard, G. W. Holmes, M. R. Lichtenstein, George C. Turner and Henry C. Sweany, Chairman.

**Dr. Ernest E. Irons, President, Dr. Herman N. Bundesen, Vice-President and Mr. Philip Weber, Secretary.

of the drug and authorized the Streptomycin Board to select cases according to medical indications.

Almost simultaneously it became evident that there were possibilities of still further reducing the dosage without a corresponding reduction of the drug's therapeutic effect. There were only two studies at the time on which we could base our judgment since the work of the Service groups and the United States Public Health Service was just getting under way. Karlson and Feldman[31] of the Mayo Clinic reported that in guinea pigs of 677-700 gms. a dosage of six to eight mg. was as effective as larger amounts. By analogy, a 50 kilogram person would do well on a dosage of 0.5 to 0.6 gram a day. Since results in animals should not be translated to humans directly we relied more on Bogen's work[32] on human beings, which demonstrated that 0.5 gram a day and even as little as 0.2 gram would heal tuberculous tracheobronchitis. Only on a dose as low as 0.1 gram did he notice any decrease of the drug's effect on the lesions. With these two studies before us we made the decision to adopt a 0.5 gram dose for all patients weighing less than 150 pounds and 0.75 gram for all patients over that weight, except in the cases of miliary, meningeal, genitourinary, bone, joint, lymph node and pericardial tuberculosis where 1 to 1.5 gram doses were continued. The value of this dosage has been substantiated by our work and by the work of the Service groups.[20]

The change in dosage had many desirable advantages. There has been to date only one case of serious labyrinth disease on the low dosage. In addition, the cost of the drug per patient was greatly reduced. There was less nursing care necessary since fewer daily doses were required.

Along with this reduction in dosage came the reduction in the length of time of treatment, first from 120 to 90 then to 60 and finally to 45 days. The Service Groups' minimum time was established at 42 days.

Justification for reducing the length of time of treatment was offered by Barnwell, Bunn and Walker[20] in human tuberculosis. These authors observed that maximum results were obtained rather early in the treatment and that prolonged treatment did not always benefit the patient. These same authors as well as Bernstein, D'Esopo and Steenken[33] indicated that the arrest of progress of the healing was partly due to resistance which was found to develop in as high as 80 per cent of the strains of bacilli during the second to the fourth month of treatment. Another important observation made by Feldman and his associates[34] and Steenken and his associates[35] was that tuberculosis produced in guinea pigs by resistant micro-organisms was not helped by

Streptomycin treatment. The work was therefore becoming increasingly complex as time went on.

The control work at our Institution was carried out along lines similar to those recommended by the Service groups and the United States Public Health Service Committee, with the exception that the laboratory and x-ray control work was usually not as closely spaced because of the lack of technical help.

Except at the beginning only the more acute types of disease, those in which there were recent infiltrative processes with or without excavation, were considered for treatment.

The obligatory haphazard method of case selection prevailing at the beginning of our work was not all in vain. We found that little permanent gain accrued from treating certain types of the disease, notably advanced caseo-pneumonic and chronic fibroid types. Although the work of Howlett and O'Connor[36] has shown that many temporary favorable clinical results may be obtained by the treatment of the chronic type of case, most of the improvement that they noticed was "not sufficiently consistent nor definite to justify wide use in the chronically active and unstable cases of pulmonary tuberculosis." Many fibroids with acute infiltrative lesions justify a short trial of the drug, especially if there is a chance for surgery. Even a relatively recent cavity may be affected and partly closed by some as yet unexplained effect on the bronchus entering the cavity. The treatment probably clears some of the inflammation around the valvular opening which automatically removes the tension, and if the wall is not too thick the cavity will collapse. In the walls of recently formed cavities the bacilli may also be attacked by the drug. In long standing chronic cases, however, especially those who are ambulant or might become ambulant without closing out the bacilli, treatment is definitely contra-indicated not only because of the ineffectual results but because of the danger of creating and disseminating resistant bacilli.

Practically all the complications of the disease and the drug treatment itself have been handled as recommended by the earlier studies, with generally similar results. We found contact dermatitis of the nurses a disturbing problem until protective measures were adapted.

The following figures and comments represent an interim report of the over-all Streptomycin program at our Institution. Final analysis will not be supplied at this time since practically all the specialties involved are to be included in more complete studies to be given later. McEnery and his associates[37] have already reported on the treatment of progressive primary tuberculosis in children. The reports on the treatment of orthopedic, proctologic,

laryngeal and enteric tuberculosis, on surgical tuberculosis and on the bacteriological studies are being prepared.

There is an insufficient number of cases of the other complications to warrant special reports as yet. Accordingly the genito-urinary, lymph node, miliary, meningitic and other organ-localized tuberculosis, as well as tuberculous sinuses and fistulae, will be included in the complete report of which this paper is only a preliminary.

In the whole series, the treated cases may be arranged into four main groups based on the degree of recovery. First, there are those which have shown no change, with the possible exception of an emphermeral improvement in subjective clinical symptoms which might even be ascribed to a psychic effect; second, those which have shown definite improvement in subjective symptoms for several days to a few weeks, but few or no other changes; third, those which have shown marked change in subjective clinical symptoms and in addition have shown clearing on the x-ray films and improvement of most laboratory tests, but only temporarily; and fourth, those which have shown considerable or marked changes of an apparently permanent nature.

Up to the present, 1,012 patients have been treated, and in 863 the treatment has been completed. Of the latter, 470 (54.5 per cent) have shown a substantial and lasting improvement. Although a few cases of extra-pulmonary tuberculosis improved when the lung lesions failed to improve, the numbers were not enough to distort the main findings. In general, this group did not include most cases suitable for primary pneumothorax and thoracoplasty, although a small number of such operated cases have been treated with Streptomycin prophylactically.

Of 670 non-surgical cases 371 (comprising 55.4 per cent of the group and 43.0 per cent of all treated cases) have shown an unmistakable favorable response; many of these have been discharged or are in the process of being discharged.

Of 371 non-surgical cases responding favorably 223 (comprising 60.1 per cent of the group and 25.8 per cent of all completed treated cases) were pulmonary and 148 (39.9 per cent of the group and 17.2 per cent of all) were non-pulmonary cases. Practically all the cases classified as "non-pulmonary" had some pulmonary disease which responded with wide variation to the administration of the drug. A correct analysis of all aspects of these cases obviously must await the complete report.

Surgery was recommended in 193 cases (22.4 per cent of all treated cases); 99 (11.5 per cent of all cases) received surgery and 66 (7.7 per cent of all cases) were prepared for surgery but have not yet been operated on. Twenty-eight (3.2 per cent of all

cases) of those which received surgery developed some postoperative complication.

Of the pulmonary cases treated, 178 were of the infiltrative or dense caseo-pneumonic types of which only 72 (40.5 per cent of the group and 8.4 per cent of all treated cases) had a more or less permanent favorable result. The poor showing of this group is due to the fact that many "palliative" cases and, particularly during the early stages of the work, cases with poor prognosis, were included. Of 202 progressive fibrocaseous and fibrocaseous and ulcerative types, 113 (55.9 per cent of the group and 13.1 per cent of all treated cases) showed a favorable result; 22 of 29 progressive primary lesions in children were permanently improved; 14 of 15 bilateral fibrocaseous and ulcerative cases with pneumoperitoneum were markedly improved, and two of seven cases of miliary tuberculosis were improved and are still living. The results on extra-pulmonary tuberculosis are shown in Table II.

The findings are what might be expected from the type of cases treated. For example, there were several seriously ill cases with far-advanced pulmonary disease in addition to the complication, who did not show anything more than temporary improvement of subjective clinical symptoms of the pulmonary process even if the complication improved. Those with broncho-pleural fistulae nearly all had cutaneous fistulae as well. Several of these combined fistulae have as yet failed to respond to treatment.

It should be pointed out also that the number shown in the table include only the cases primarily selected for the treatment of the complication irrespective of other disease present. For example, there were only six cases selected for treatment of ano-rectal tuberculosis, but there are 18 other cases having ano-rectal

TABLE I

Pulmonary Tuberculosis (Non-Surgical) Treated With Streptomycin

TYPE OF DISEASE	— RESULTS —	
	Favorable	Temporary or No Improvement
1. Acute infiltrative or caseo-pneumonic	72 (42.8%)	96
2. Progressive lesions (fibrocaseous and/or ulcerative)	113 (55.9%)	89
3. Streptomycin with pneumoperitoneum	14 (93.3%)	1
4. Progressive primary in children	22 (71.0%)	9
5. Miliary	2 (22.2%)	7
TOTAL	223 (52.5%)	202
GRAND TOTAL		425

complications in cases treated for pulmonary disease, enteritis, etc. A complete presentation of every aspect of each case must wait the report of the various specialties and a complete analysis of all the data.

Without including the 66 cases who have not yet received surgery, there were 470 cases (54.5 per cent) who have been improved to such an extent that many have already been discharged as "arrested"; many are in good condition and are being prepared for discharge, and the remainder have improved from a poor to a good prognosis. Subsequently, a large number of the 66 cases prepared for surgery but not yet operated on, some of the 28 cases having postoperative complications and a few of the 23 cases who have had retreatment with Streptomycin or Dihydrostreptomycin will probably recover.

Any attempt to determine the net gain of our Streptomycin Program is practically impossible at this time. An approximation of the figures for this type of hospital, however, may be made by comparing the combined percentage of recovery of the Streptomycin treated non-surgical cases and the surgical cases whose surgery was made possible solely by the use of Streptomycin, with the percentage of recovery of all moderate and far-advanced cases in previous years who did not have any form of surgery. It may be stated conservatively that over 50 per cent of properly

TABLE II

Extra-Pulmonary Tuberculosis Treated With Streptomycin

TYPE OF DISEASE	— RESULTS —	
	Favorable	Temporary or No Improvement
I. Tuberculosis of the mucous membranes		
(a) Tracheobronchitis	29 (52.7%)	26
(b) Laryngitis	72 (69.2%)	32
(c) Enteritis	13 (54.1%)	11
(d) Rectal	6 (100%)	0
II. Tuberculosis of bones and joints	7 (63.6%)	4
III. Genito-urinary tuberculosis	9 (90 %)	1
IV. Tuberculous Lymphadenitis	4 (44.4%)	5
V. Broncho-pleural Fistulae	7 (36.8%)	12
VI. Tuberculous Meningitis	1 (14.3%)	6
TOTAL	148 (60.4%)	97
GRAND TOTAL		245

selected cases were improved in a permanent way. Since the total number of treated cases represented about 40 per cent of all admissions (after the full scale program was established) the cases receiving permanent benefit were approximately 20 per cent.

If, as the figures seem to indicate, there is real gain in Streptomycin treatment, that gain must ultimately be reflected in a decreased death rate. At the present time, a more obvious indicator is that the hospital stay of some of the treated cases is reduced to about one-half or one-third of the time required for the same type of case left untreated.

One of the greatest problems confronting us at the beginning of our program was the prolongation of lives of hopeless cases for weeks or months, which created serious shortage of beds needed for the more urgent treatable cases. We finally were forced to refrain from treating unmistakably hopeless cases, except as a palliative measure.

Although an absolute clinical improvement was proved rather early in the Streptomycin Program, the pathological changes resulting from Streptomycin treatment in human tuberculosis had to wait some time for an understanding because the material was rather slow to accumulate. The pathology is of two types, viz: that due to toxicity of the drug and that due to the effect of the drug on the tuberculosis.

The pathology of the labyrinth disease is still obscure. Fowler[38] has felt that it is due to the nerve nucleus damage. The effect of the drug on the lesions is more definite, but many features are not yet classified. The effect on the kidney is even more indefinite.

The effect on the lesions in the brain is apparently not constant. Baggenstoss, Feldman and Hinshaw[39] found that in one case there was an apparent stimulation of tubercle formation resulting in a sort of tuberculous encephalitis. They felt this stimulation was due to the low concentration of Streptomycin since they could recover very little Streptomycin from the brain. Rhymer and Wallace[40] confirm these findings. Baggenstoss, Feldman and Hinshaw[39] showed healing of tubercles similar to those found elsewhere in the body. The most complete work on the pathology of the central nervous system is that of Zollinger[41] who showed that a fibroid condition develops in the patients who survive a long time. The fibrous tissue causes a closure of the subarachnoid spaces, resulting in hydrocephalus. An endophlebitis results in a red encephalomalacia, and an endarteritis, a white encephalomalacia. Practically all workers agree that there is marked effect on recent small tubercles. There is a "withering" effect on the monocytic cells around the periphery, a decrease in caseation and a gradual supplanting of the caseous centre by

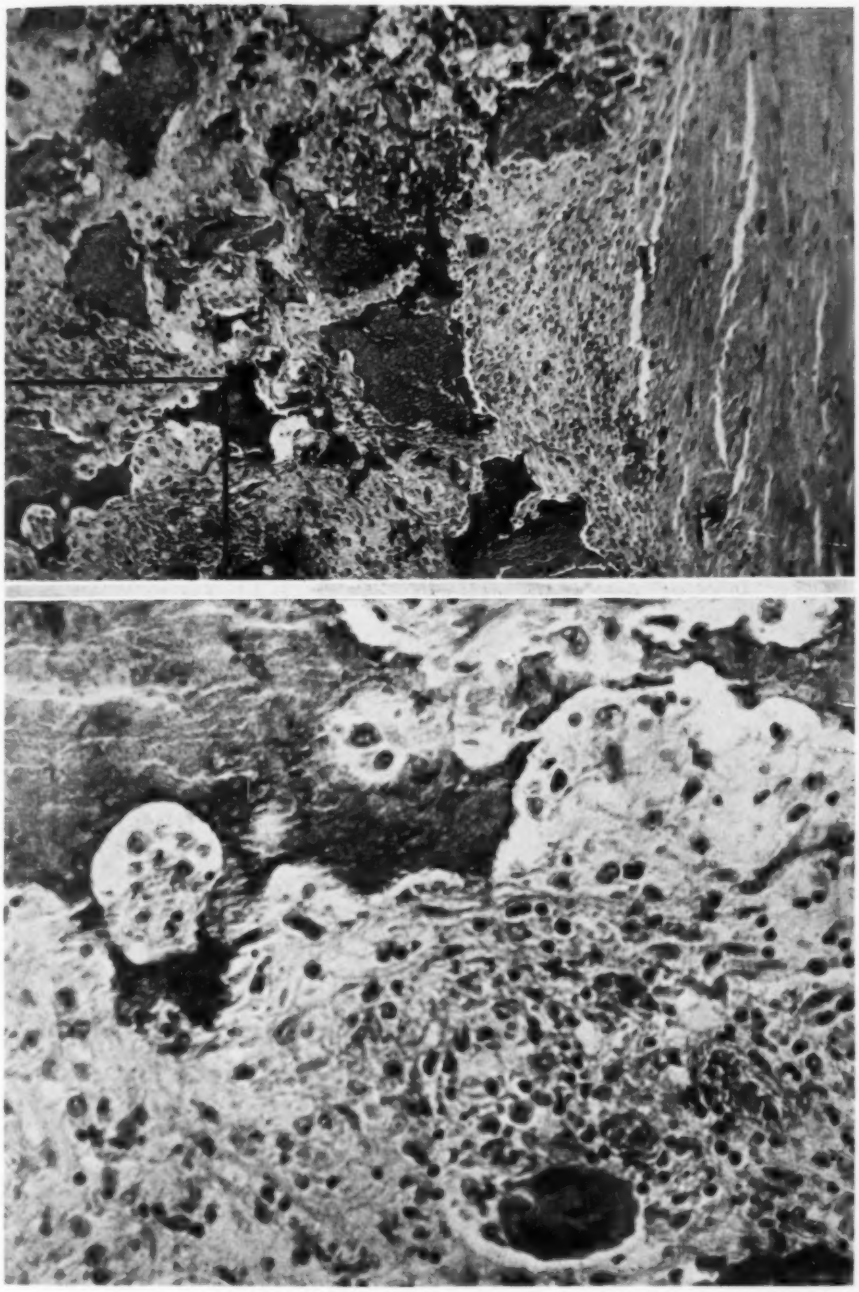


FIGURE 1

Fig. a: A low power view of a calcified hilum lymph node in Case I. Heavy fibrous capsule on the right and broken islands of calcification beneath. x 30, H. and E. *Fig. b:* A higher magnification of a portion of Fig. a outlined in rectangle. Note the invasion of "phage" cells into the calcified islands, a condition rarely seen before 8-10 years. x 200 H. and E.

fibroblasts and fibrous tissue. Many old tubercles thus healed appear only as scars of fibrous tissue.

The following cases will illustrate several types of change in tubercles from different parts of the body. While the changes in many tubercles are not remarkable, those of primary lesions and those of the liver are rarely seen in ordinary terminal cases.

Case 1: W.B., a three year old white male, was first brought into the Children's Memorial Hospital with what was thought to be a terminal condition, having far-advanced lung disease and draining neck sinuses.

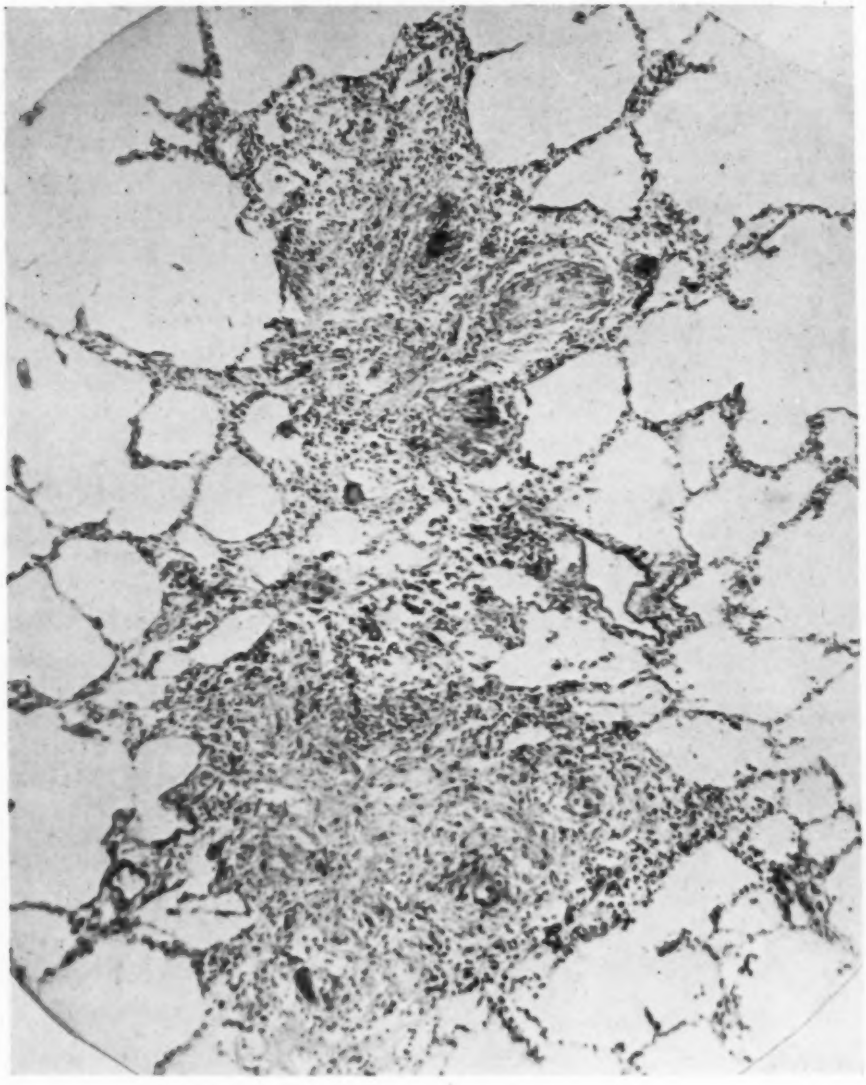


FIGURE 2

A low power view of a miliary tubercle in the lung of the same case. Note the withered epitheliod and giant cells and the replacement of the caseous center with fibroblasts. x 30 H. and E.

He was started on large doses of Streptomycin and almost immediately transferred to our hospital where the treatment was continued but on lower dosage. The almost moribund child gradually improved, became afebrile and alert, gained weight, his sinuses healed and he finally was allowed liberty around the ward. In the meantime, the roentgenograms revealed a considerable clearing in the lungs. Then, suddenly he became nauseated and developed other signs of meningitis, from which he expired within two weeks.

Necropsy: Death was caused by an ordinary basal meningitis which developed from a Streptomycin resistant strain of tubercle bacilli.

The lungs were remarkable in that they presented marked healing in a far-advanced and ulcerative tuberculosis. There was an excavation of most of the middle lobe with a residue of calcified caseous material around the margins and numerous gravelly concretions in all the interstices of the cavity. The calcified foci appeared to be of greater age than ever seen before in a three year old child. The cavity generally had a smooth wall, some of which was becoming relined with epithelium. Another large and more rceent cavity that had contracted to about a third of its former size was present in the right upper lung lobe. There

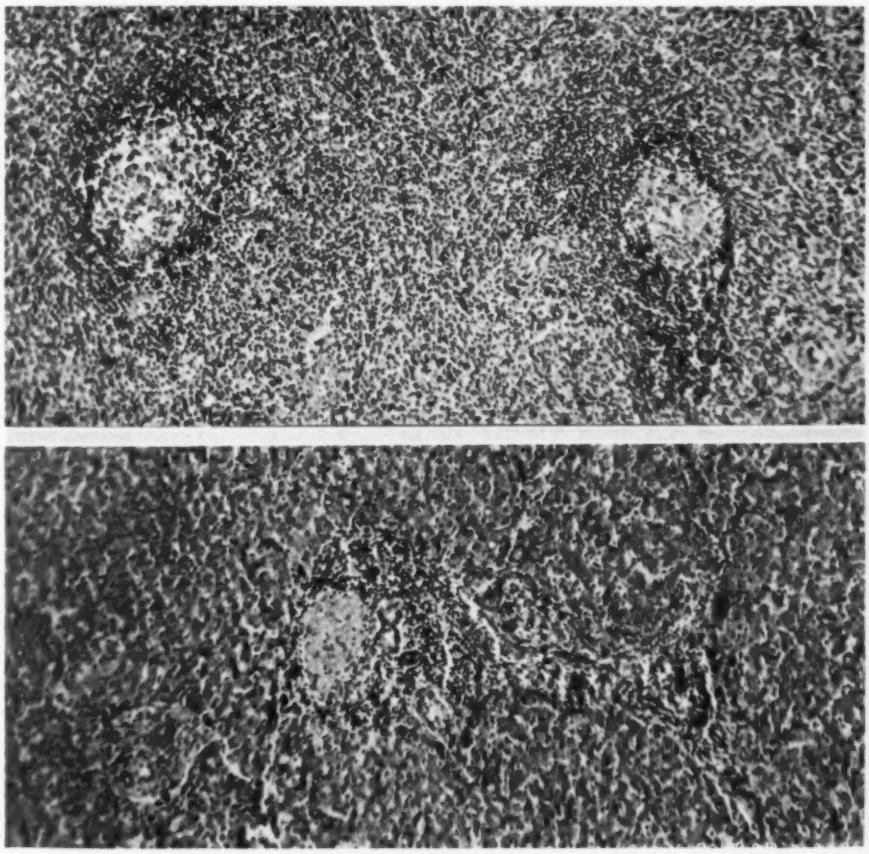


FIGURE 3

Fig. a: A low power view of a section of the spleen of the same case. Note the remnants of miliary tubercles as fibrous tufts in the Malphigian corpuscles. *Fib. b:* Same type of formation in the liver. x 30 H. and E.

was practically no pyogenic layer left, and much fibrosis was present in the walls of the cavity. In the left upper lung lobe there were many tubercles heavily encapsulated and calcified.

Microscopic Examination: Hilum lymph node tubercle: A decalcified and stained section of a primary hilum lymph node tubercle presented a mass of broken calcified islands with marked resorption, which has been described earlier, and a replacement of the resorbed areas with fibroblasts and capillaries. No bone or fibro-ostioid tissue was present, but the changes were those normally seen only after six to seven years time.

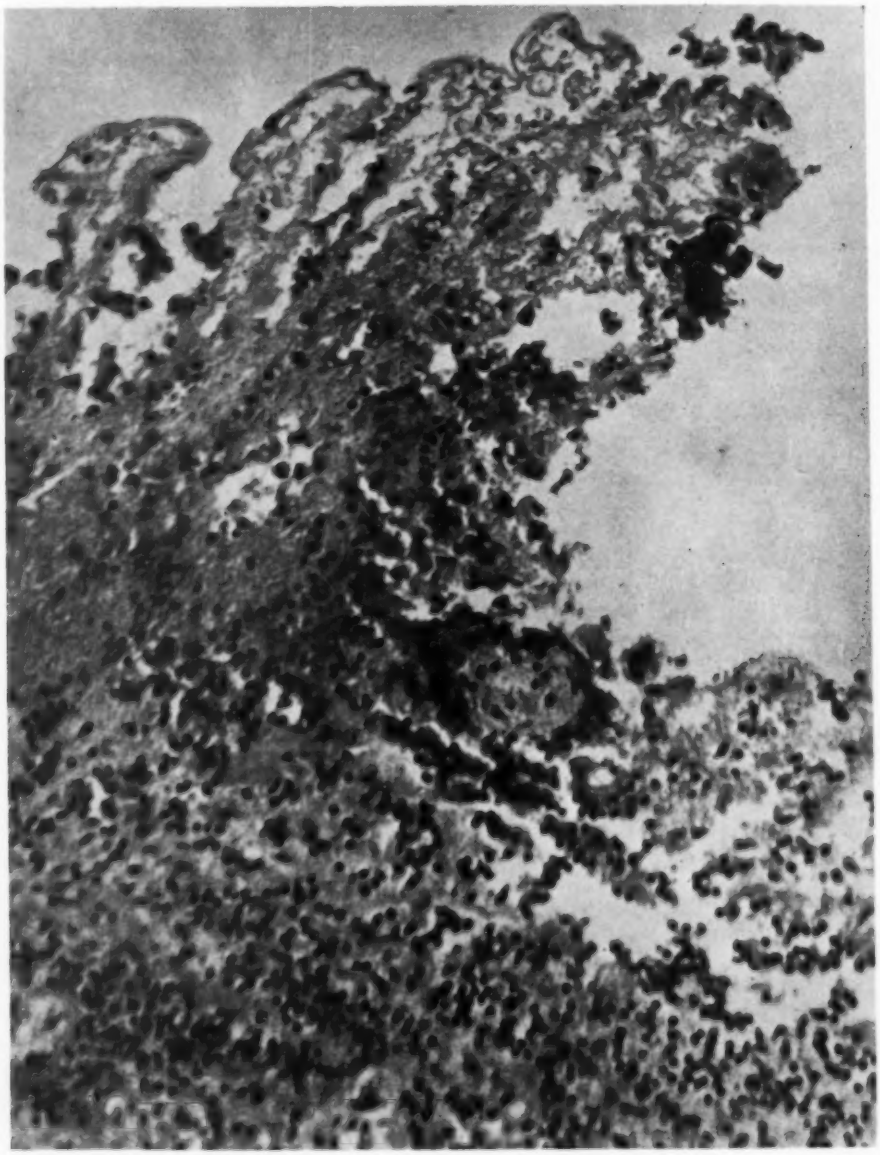


FIGURE 4

A view of the border of an ulcer in the ileum. Note the withered epitheliod cells and giant cells, with lymphocytes beneath the floor of the ulcer. x 50 H. and E.

It was the impression that healing was about twice as rapid as seen in ordinary healing tubercles (Fig. 1).

Other changes in the lymph nodes were markedly regressive, with fibrosis and a disappearance of caseation, but were not different from those that have been seen in healing lesions without Streptomycin. The lesions in the lung parenchyma were of two types: the miliary, showing a skeleton tubercle enclosed in the capsule of fibrosis, and almost complete resorption of the caseation. Occasionally there was an obsolete or changed giant cell. The other type, or larger tubercle, seemed to be altered around the periphery, especially if recent, revealing a pyknosis and "withering" of the epitheloid cells but not remarkable in the deeper aspect of the tubercle (Fig. 2).

In the spleen were accumulations of lymphocytes with a few interlacing fibroblasts in the malphigian corpuscles which were thought to be healing and healed tubercles. The writer has never before observed as many of these healed lesions in a spleen (Fig. 3a).

In the liver there were a few fibroid tufts that presumably were at one time miliary tubercles which had undergone healing similar to the healing described of the lesions in the spleen (Fig. 3b).

The gastro-intestinal tract is probably the most interesting, since few reports have been made on healed lesions in these organs. The whole mucosa was a fused mass of stroma, fibroblasts and an occasional "blind" duct with only a few mucosal cells remaining. A small ulcer with overhanging edges had a few old giant cells around the margins but only a slight infiltration of lymphocytes in the base of the ulcer. The whole picture was that of removal of inflammatory elements with little or no replacement of fibrous tissue.

It was the feeling that the healing present had been speeded greatly by the treatment with Streptomycin (Fig. 4).

Case 2: A 55 year old male was ill with tuberculosis since January 1946 and was treated with pneumothorax in 1946 and with thoracoplasty on the right side in 1947. In July 1948 he had a spread to the left lung and in addition he had a tuberculous epididymitis. (Streptomycin (0.5 gm. daily) was begun on August 24, 1948, and continued until October 26, 1948. There was a considerable improvement, but on December 6, 1948, he developed signs of meningitis (rigidity of the neck, positive Kernig, etc.), and on December 8, 1948, treatment with Dihydro-streptomycin was begun; 3 gm. daily and 25 micrograms intrathecally three times a week. He expired nine days later.

The essential features were a post-thoracoplasty right lung, with a "healing emphysema" in the left lung. The tubercles were mostly dry, caseous and encapsulated. The epididymi were both filled with caseation and free flowing pus; the vas deferens on each side also contained pus. There were many small nodules in the kidneys. The cerebellum contained several yellow gray areas of several mm. in diameter. The largest measured 12 mm. in greatest dimensions. The other organs presented nothing remarkable.

The tubercles in the liver especially showed a remarkable degree of fibrosis; a heavy band of collagenous connective tissue was present around a small area of pale caseous material. In fact, some of the tubercles were almost entirely filled with fibrous tissue. The tubercles in the lungs appeared to be undergoing healing, but there was nothing that would not be found in any healing tuberculous process.

The cerebellar tubercles were rather unusual in that the periphery of monocytes had a "scorched" or "frost bitten" appearance with some fibroblasts beginning to form around the outer margin. The impression was gained that the effect was recent and perhaps due to the Streptomycin.

Discussion

One of the remarkable features of Streptomycin studies is the rapidity with which the work is progressing. Every week brings out some new and improved aspect of the treatment. Already, Dihydro-streptomycin is being prepared in quantity and has been found to produce little or no ear damage in doses less than 2 grams a day. Dihydro-streptomycin, however, according to work of Feldman and others[42] does not insure protection against resistance to Streptomycin. Other combinations of drugs are being used to supplement Streptomycin when resistance to the drug prevents further curative effect. Sulphones have been used by Debré,[24] Cocchi[23] and others, and promizole has been used in meningitis by Lincoln.[43] Iodides have been used by Woody and Avery[44] in chronic tuberculosis. We have used Paramino-salicylic acid with some success after Streptomycin has failed. Vannesland, Ebert and Block[45] have shown experimentally that the use of P.A.S. with Streptomycin is better than that of either drug alone. It is desirable that an accessory drug be found to take over the action by the time the bacillus has gained resistance to Streptomycin.

Before closing, a few words of caution should be offered. First is a warning against too large a dosage of Streptomycin. The trend from the beginning has been to reduce both dosage and time of treatment. The dosage we use approaches an ideal where the greatest benefit is obtained with the least damage. This work has supported the work of others[24,20] who have reported that good results can be obtained by 0.5 to 1.0 gram dosage. While those who have had adequate experience with the drug have already learned how to avoid most ear complications, all too many have continued to give as large as two to three grams daily, which is almost certain to leave cripples even if the disease is controlled. Furthermore, it is not yet safe to rely too much on Dihydro-streptomycin because it is not always exempt from danger, especially in dosage over two grams a day.

Much more serious is the problem of germ resistance. We cannot escape the conclusion that after a few years our new infections will be due largely to resistant bacilli for which no remedy is now available. Already some cases are appearing. Therefore, the random use of Streptomycin on minimal lesions or fibro-ulcerative types in which the indications are slight or dubious, as judged by

vast experiments already performed, should be discouraged and where possible forbidden. Exception should be made when such cases are amenable to surgery, for the drug may here be used with advantage, both in preparing the patient and in prevention of post-surgical exacerbation of the tuberculosis.

The final results of Streptomycin treatment are still speculative, but enough has already been accomplished to aid materially in the solution of the tuberculosis problem, and it is not too much to expect a still better method of therapy within five years or less.

No better concluding remarks could be made than to repeat the words of Waksman,[3] namely: "A turning point has now been reached in the chemotherapy of tuberculosis. Although Streptomycin may not be the final answer in the treatment of this scourge of mankind—and I hope that it is not—it has opened a new path of antibiotic approach to chemotherapy, an approach sought since the discovery of the bacterial nature of the disease; the control of tuberculosis may finally materialize and thus advance man one step further in his battle against disease and epidemics."

SUMMARY AND CONCLUSIONS

A brief and incomplete summary of the beginning and development of Streptomycin work over the world, including important features of our own work, has been presented. The essential features may be enumerated as follows:

1) Streptomycin "suppresses" the growth of practically all strains of tubercle bacilli for periods of several weeks to several months.

2) During that period of time there is a large number of cases changed from poor to a good prognosis; this will be reflected ultimately in a lowered death rate and a shortening of the time of individual convalescence.

3) Resistance to Streptomycin develops partially or completely in about 80 per cent of strains of tubercle bacilli on or before 120 days of treatment.

4) Recently formed lesions (probably those retaining blood circulation) respond the most favorably to treatment with Streptomycin; lesions respond less favorably as they become more caseous or more fibroid in character.

5) At the present time, indications are that the optimum dosage of Streptomycin is around one gram a day, although 0.5 of a gram a day has been used with success.

6) In our work we have used a dosage regimen of 0.5 gram a day on adult patients under 150 pounds, and 0.75 gram a day on those over 150 pounds, for 45 to 120 days or up to the time of development of bacilliary resistance. In infants and children under

50 pounds 0.1 to 0.3 grams has been found adequate. Only one case of labyrinth disease has developed on this regimen.

7) Of 863 cases in which treatment was completed, using the 0.5 to 0.75 gram dosage, 470 cases (54.5 per cent) were improved in a substantial and more or less permanent way; have gone on to recovery; are progressing towards recovery; or have undergone surgery.

8) There were 670 (77.6 per cent of all cases) non-surgical cases, 425 of which were pulmonary (63.3 per cent of the latter group and 49.3 per cent of all cases). Of these pulmonary cases, 223 (52.5 per cent of the group and 25.9 per cent of all cases) were improved. Of the remainder of the non-surgical cases, 245 (28.3 per cent of all cases) were non-pulmonary, with 148 (60.4 per cent of the latter and 17.2 per cent of all cases) showed improvement.

9) Surgery was recommended in 193 (22.4 per cent of all treated) cases, of which 99 have been operated on successfully and 28 have been operated on but have had postoperative complications; 66 cases have refused surgery or the operation has been delayed for one reason or another.

10) On meningeal, miliary, bone, joint and genito-urinary lesions, 1.0 to 1.5 grams of Streptomycin is still recommended, but Dihydrostreptomycin in doses up to two grams is preferred because of its lower neuro-toxicity.

11) The basic pathologic change in the tubercle is in the reduction of monocytes and epitheloid cells; the decrease and perhaps cessation of caseation with a gradual fibrotic replacement of the central caseation and a thickening of the capsule of the tubercle. In primary calcified tubercles there is a marked acceleration of calcification and resorption of the calcification with replacement by fibroblasts, collagenous tissue and capillaries.

12) In the lesions of the intestinal mucosa where the epithelium is largely destroyed, the first changes observed are the disappearance of acute inflammatory cells and a withering of the epithelioid and giant cells from the floors of the ulcers with only a few lymphocytes remaining. Later changes have not yet been observed, but it is presumed that fibroblasts and fibrocytes appear in order and ultimate re-epithelialization takes place.

13) The types of lesions in the central nervous system are quite varied, depending on many factors such as the type of the disease, duration of the disease before treatment, the development of fibrous tissue, and development of bacilliary resistance. In partly healed lesions fibrous tissue may block the subarachnoid spaces, causing hydocephalus; basalar endarteritis and endophlebitis may lead to white and red encephalomalacia respectively. Small tubercles may heal by fibrosis as do lesions elsewhere in the body or

there may be exacerbations of caseous and fibrocaseous lesions in the meninges, mostly in its basal region.

14) There is nothing specific in the pathologic changes caused by Streptomycin.

RESUMEN Y CONCLUSIONES

Se presenta un breve e incompleto resumen de los comienzos y evolución del trabajo sobre la Estreptomicina en el Mundo, incluyendo los hechos importantes de nuestro trabajo personal.

Los puntos esenciales pueden ser enumerados como sigue:

1) La Estreptomicina "suprime" el crecimiento de practicamente todas las cepas de bacilos tuberculosos por periodos desde varias semanas hasta varios meses.

2) Durante este periodo de tiempo hay un gran número de casos que cambian de malo a buen pronóstico; esto se reflejará a la postre en una mortalidad menor y en acortamiento del tiempo de la convalescencia individual.

3) La resistencia a la Estreptomicina se desarrolla parcial o completamente en aproximadamente 80 por ciento de las cepas del bacilo tuberculoso dentro o antes de 120 días de tratamiento.

4) Las lesiones recién formadas (probablemente las que conservan circulación sanguínea) responden más favorablemente al tratamiento con Estreptomicina; las lesiones responden menos favorablemente a medida que son más caseosas o de carácter más fibroso.

5) En el momento actual hay indicaciones de que la dosis óptima de Estreptomicina es alrededor de 1 gmo. por día aunque 0.50 por día se ha usado con éxito.

6) En nuestro trabajo hemos usado una dosificación de 0.50 gms. por día en enfermos pesando menos de 150 libras y 0.75 gms. por día en los que sobrepasan 150 libras, por 45 a 120 días o hasta que se desarrolla la resistencia bacilar. En bebés y en niños con menos de 50 libras 0.10 a 0.30 se ha encontrado adecuado. Solo se ha encontrado un caso de afección del laberinto con esta dosificación.

7) De 863 casos en los que el tratamiento se ha terminado usando la dosificación de 0.50 a 0.75 gms., 470 (54.5 por ciento) mejoraron de un modo evidente y de modo más o menos permanente, han marchado hacia la recuperación, están en vías de obtenerla o se han sujetado a la cirugía.

8) Hubo 670 (77.6 por ciento) de todos los casos no quirúrgicos, de los cuales 425 eran pulmonares (63.3 por ciento del último grupo y 49.3 por ciento de todos los casos). De estos casos pulmonares 223 (52.5 por ciento del grupo y 25.9 por ciento de todos los casos) no eran pulmonares, con 148 (60.4 por ciento de los

últimos y 17.2 por ciento de todos los casos) que mostraron mejoría.

9) Se recomendó la cirugía a 193 (22.4 por ciento de todos los tratados) de los que 99 han sido operados con éxito y 28 han sido operados, pero tuvieron complicaciones postoperatorias; 66 rehusaron las operaciones o la operación ha sido diferida por una u otra causa.

10) En la tuberculosis meníngea, miliar, ósea, articular y genito urinaria se recomiendan aún dosis de 1.00 gmo. a 1.50, pero la Dihidroestreptomicina en dosis hasta de 2 gmos. es preferida por su neurotoxicidad más baja.

11) El cambio histológico en el tubérculo básicamente es la reducción de los monocitos y de las células epitelioides; el decrecimiento y quizás la suspensión de la caseificación con una substitución por fibrosis de la caseificación central y el engrosamiento de la cápsula del tubérculo. En los tubérculos primarios hay una marcada aceleración de la calcificación y reabsorción de la calcificación con substitución por fibroblastos, tejido colágeno y capilares.

12) En las lesiones de la mucosa intestinal donde el epitelio es ampliamente destruído, los primeros cambios observados son la desaparición de las células inflamatorias agudas y el decrecimiento de las celdillas epitelioides y gigantes en el fondo de las úlceras, quedando solo algunos linfocitos. Cambios ulteriores no se han observado aún pero se supone que aparecen fibroblastos y fibrocitos y que después se realiza una re-epitelización.

13) Los tipos de lesiones del sistema nervioso central son muy variados, dependiendo de muchos factores tales como el tipo de la enfermedad, duración de ella antes del tratamiento, el desarrollo de tejido fibroso y el desarrollo de resistencia bacilar. En las lesiones parcialmente curadas el tejido fibroso puede bloquear los espacios subaracnoideos, causando hidrocefalia; la endarteritis y la endoflebitis basilar pueden conducir a encefalomalacia blanca o roja respectivamente. Los pequeños tubérculos pueden curar por fibrosis como las lesiones en cualquier parte del cuerpo o puede haber exacerbaciones de lesiones caseosas o fibrocaseosas en las meninges, especialmente en su región basal.

14) No hay nada específico en los cambios patológicos producidos por la Estreptomicina.

REFERENCES

1 Domagk, G.: "Ein Beitrag zur Chemotherapie der bakteriellan Infektionen," *Deutsche med. Wchnschr.*, 61:250-253, (Feb. 15) 1935.
2 Fleming, Alexander: "On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to Their Use in the Isolation of B. Influenzae," *Brit. J. Exper. Path.*, 10:226-236, (June) 1929.
3 Waksman, Selman A.: "Antibiotics and Tuberculosis, A Microbiologic Approach," *J.A.M.A.*, V. 135:478-485, (Oct.) 1947.
4 Schatz, Albert, Bugie Elizabeth and Waksman, S. E.: "Streptomycin,

a Substance Exhibiting Antibiotic Activity Against Gram-Positive and Gram-Negative Bacteria," *Proc. Soc. Eper. Biol. and Med.*, 55:66-69, (Jan.) 1944.

5 Feldman, W. H. and Hinshaw, H. C.: "Effects of Streptomycin on Experimental Tuberculosis in Guinea Pigs: A Preliminary Report," *Proc. Staff Meet., Mayo Clinic*, 19:593-599, (Dec. 27) 1944.

6 Feldman, W. H., Hinshaw, H. C. and Mann, F. C.: "Streptomycin in Experimental Tuberculosis," *Am. Rev. Tuberc.*, 52:269-298, (Oct.) 1945.

7 Hinshaw, H. C. and Feldman, W. H.: "Streptomycin in Treatment of Clinical Tuberculosis: A Preliminary Report," *Proc. Staff Meet., Mayo Clinic*, 20:313-318, (Sept. 5) 1945.

8 Heilman, D. H., Heilman, F. R., Hinshaw, H. C., Nichols, D. R. and Herrell, W. E.: "Streptomycin: Absorption, Deffusion, Excretion and Toxicity," *Am. J. M. Sc.*, 210:576-584, (Nov.) 1945.

9 Baggenstoss, A. H., Feldman, W. H. and Hinshaw, H. C.: "The Effect of Streptomycin on the Pathology of Generalized Miliary Tuberculosis of Human Beings," *Am. Rev. Tuberc.*, V. 55:154-75, (Jan.) 1947.

10 Cooke, R. E., Dunphy, D. L. and Blake, F. G.: "Streptomycin in Tuberculosis Meningitis; A Report of Its Use in a One-Year-Old Infant," *Yale J. Biol. and Med.*, 18:221-226, (Jan.) 1946.

11 Moersch, H. J., Clagett, C. T., Wood, H. G., Schmidt, W. H., Olsen, A. M. and Carr, D. T. of the Mayo Clinic; Petersen, Magnus of Rochester State Hospital, and Burns, H. A. of the Division of Public Institutions of the State of Minnesota.

12 Figi, F. A., Hinshaw, H. C. and Feldman, W. H.: "Treatment of Tuberculosis of the Larynx with Streptomycin: Report of Case," *Proc. Staff Meet., Mayo Clinic*, 21:127-130, (March 20) 1946.

13 Cook, E. N., Greene, L. F. and Hinshaw, H. C.: "Streptomycin in the Treatment of Tuberculosis of the Urinary Tract," *Proc. Staff Meet., Mayo Clinic*, 21:277-280, (July 24) 1946.

14 O'Leary, P. A., Ceder, E. I., Hinshaw, H. C. and Feldman, W. H.: "The Treatment of Various Types of Cutaneous Tuberculosis with Promizole and with Streptomycin: A Preliminary Report," *Arch. Dermat. and Syph.*

15 Youmans, G. P., Williston, Elizabeth H., Feldman, W. H. and Hinshaw, H. C.: "Increase in Resistance of Tubercle Bacilli to Streptomycin: A Preliminary Report," *Proc. Staff Meet., Mayo Clinic*, 21:126, (March 20) 1946.

16a McDermott, W., Muschenheim, C., Hadley, Susan J., Bunn, P. A. and Gorman, Rosemary V.: "Streptomycin in the Treatment of Tuberculosis in Humans: 1. Meningitis and Generalized Hematogenous Tuberculosis," *Ann. Int. Med.*, 27:769-822, (Nov.) 1947.

b Muschenheim, C., McDermott, W., Hadley, Susan J., Hull-Smith, Harriet and Tracy, Alice: "Streptomycin in the Treatment of Tuberculosis in Humans: II. Pulmonary Tuberculosis," *Ann. Int. Med.*, 27: 989-1027, (Dec.) 1947.

17 Barnwell, J. B., Bunn, P. A. and Walker, A. M.: "The Effect of Streptomycin Upon Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 56:485-507, (Dec.) 1947.

18a Youmans, G. P. and Karlson, A. G.: "Streptomycin Sensitivity of Tubercle Bacilli," *Am. Rev. Tuberc.*, 55:529-535, (June) 1947.

b Williston, Elizabeth H. and Youmans, G. P.: "Streptomycin Resistant Strains to Tubercle Bacilli. Production of Streptomycin Resistance in Vitro," *Am. Rev. Tuberc.*, 55:536-539, (June) 1947.

19 Wolinsky, E., Reginster, A. and Steenken, W. Jr.: "Drug-Resistant Tubercle Bacilli in Patients Under Treatment with Streptomycin," *Am. Rev. Tuberc.*, 58:335-343, (Sept.) 1948.

20 Council on Pharmacy and Chemistry: "Streptomycin in the Treatment of Tuberculosis. Current Status. Report to the Council," *J.A.M.A.*, 138:584-593, (Oct.) 1948.

21 Bunn, P. A.: "One Hundred Cases of Miliary and Meningeal Tuberculosis Treated with Streptomycin," *Am. J. Med. Sc.*, 216:286-315, (Sept.) 1948.

22 Amberson, J. B. and Stearns, W. H.: "Streptomycin in the Treatment of Tuberculosis," *Ann. Int. Med.*, 29:221-228, (Aug.) 1948.

23 Cocchi, Cesare and Pasquinucci, Gaetano: "Primi resultati nella terapia delle meningiti tubercolari con la streptomicina associata a solfone e vitamina A," *Revista di Clinica Pediatrica*, 45:193, (Apr.) 1947.

24 Debré, R., Thieffry, et Brissaud, E.: "Méningite tuberculeuse et tuberculose miliare aigue chez l'enfant traité par la streptomycine," *Presse Med.*, 56:121, (Sept. 1) 1947.
25 Decourt, J.: "En 72 cases de méningite tuberculeuse traités par la streptomycine," *Presse Med.*, 56:129, (Feb.) 1948.
26 DeLavergne, V.: "Le centre de streptomycine de Nancy," *Presse. Med.*, 56:132, (Feb.) 1948.
27 Bernard, Etienne, Kreis, B. and Lotte, Alice: "Sur la traitemente de la tuberculose de l'adult par la streptomycine," *Presse Med.*, 56:118, (Feb. 1948.
28 Van Goidsenhoven, Fr., Stevens, R. and Crolla, P.: "La streptomycine dans la méningite tuberculeus et dans la tuberculose miliare aigué," *Bull. de L'Accad. Roy de Med. de Belg.*, 13:292-311, 1948.
29 Marshel, et al.: "Streptomycin and tuberculous meningitis," *Lancet*, 254:583, (Apr. 17) 1948.
30 Loeffler, W. and Piotti, A.: "Streptomycine und tuberkulose," *Basel*, pp. 55-126, 1948.
31 Karlson, A. G. and Feldman, W. H.: "The Subeffective Dose of Streptomycin in Experimental Tuberculosis of Guinea Pigs," *Am. Rev. Tuberc.*, 58:129-133.
32 Bogen, Emil: Personal communication regarding articles to appear in Medical Clinics of North America, March 1949, and other publications.
33 Bernstein, Sidney, D'Esopo, N. and Steenken, Wm. Jr.: "Streptomycin Resistant Tubercle Bacilli," *Am. Rev. Tuberc.*, 58:344-352, (Sept.) 1948.
34 Feldman, Wm. H., Karlson, Alfred G. and Hinshaw, Corwin H.: "Streptomycin Resistant Tubercle Bacilli; Effects of Resistance on Therapeutic Results in Tuberculous Guinea Pigs," *Am. Rev. Tuberc.*, 57:162-174, (Feb.) 1948.
35 Steenken, Wm., Wolinsky, Emanuel: "Streptomycin in Experimental Tuberculosis: Response in Guinea Pigs Infected with Strains of Varying Degrees of Streptomycin Resistance," *Am. Rev. Tuberc.*, 58:353-362, (Sept.) 1948.
36 Howlett, Kirby S. Jr. and O'Connor, John B.: "Treatment of Tuberculosis with Streptomycin: Response of Certain Subacute and Chronic Types," *Am. Rev. Tuberc.*, 58:139-172, (Aug.) 1948.
37 McEnery, Eugene, Sweany, Henry C. and Turner, George C.: "The Treatment of Progressive Primary Tuberculosis in Children with Streptomycin," In press.
38 Fowler, E. P. and Seligman, E.: "Otic Complications of Streptomycin," *Jour. Amer. Med. Ass'n.*, 133:87-91, 1947.
39 Baggenstoss, A. H., Feldman, W. H. and Hinshaw, H. C.: "The Effect of Streptomycin on the Pathology of Generalized Miliary and Minengeal Tuberculosis," *Proc. Mayo Clinic*, 22:265-274, 1947.
40 Rhymer, I. and Wallace, G. I.: "Studies on the Mode of Action of Streptomycin: The Nature of a Streptomycin Inhibitor Occurring in Brain Tissue and Plant Extracts," *Jour. Bact.*, 54:521-526, 1947.
41 Zollinger, H. U.: "Streptomycin und Tuberculose," *Basel*, pp. 293-337, 1948.
42 Feldman, Wm. H., Karlson, Alfred G. and Hinshaw, H. Corwin: "Dihydro-Streptomycin: Its Effect on Experimental Tuberculosis," *Amer. Rev. Tuberc.*, 58:525-530, (Nov.) 1948.
43 Lincoln, E. M., Krimse, T. W. and DeVito, E.: "Tuberculous Meningitis in Children: A Preliminary Report of Its Treatment with Streptomycin and Promizole," *J.A.M.A.*, 136:593-597, 1948.
44 Woody, Edgar Jr. and Avery, Roy C.: "The Combined Effect of Potassium Iodide and Streptomycin on Established Tuberculosis in Guinea Pigs," *Science*, 108:501-502, (Nov. 5) 1948.
45 Vannesland, K., Ebert, R. H. and Block, R. G.: "In Vitro Effect of Streptomycin and Para-amino-salicylic Acid (P.A.S.) on the Growth of Tubercle Bacilli," *Proc. Exp. Biol. Med.*, 68:250-255, 1948.

A Synthesis of the Prevailing Patterns of the Bronchopulmonary Segments in the Light of Their Variations*

EDWARD A. BOYDEN, Ph.D. (Med. Sc.)
Minneapolis, Minnesota

During the last four years the writer and his associates have been analyzing and mapping the arrangement and distribution of bronchial and vascular trees within the lungs, lobe by lobe. At least fifty specimens of each lobe (and in some cases a hundred or more) have been carefully dissected and sketched. These, in turn, have been supplemented by fresh specimens injected with colored gelatins.

Hitherto, published figures have been faithful replicas of original specimens, but now for purposes of instruction it has seemed desirable to create a hypothetical pair of lungs that would combine the prevailing patterns of all the segments—assembly drawings, as it were, to illustrate not only the arrangement of structures at the hilum, but also the projections onto the surface of the principal bronchi.

Probably such "ideal" specimens are only occasionally encountered, for a variation in even one zone necessarily modifies the development of adjacent segments; and the lungs are the most plastic of all organs. Hence the greater need for an empirically established pattern by which deviations may be judged. Accordingly these plates are presented in the hope that when the simpler plan has been mastered the reader will turn to the studies listed in the bibliography for a more detailed record of the struggle for space that has been waged by the embryonic bronchial buds.

Figure 1 shows an orthodox plan of the bronchial tree with ten major (i.e. segmental) bronchi on the right and nine on the left. The reduction in number of segments in the left lung is due to the union of apical and posterior bronchi ($B^{1\ plus\ 3}$). As will be pointed out later, this change involves much more than possession of a common stem, namely an "elision" of these bronchi. Many authors also consider that the medial basal and anterior basal bronchi of the left lung (B^7 and B^8) aerate a single segment. But in a study of sixty left lower lobes[1] it has been shown that these two bronchi maintain their identity and do not form a composite stem as so often happens in the case of $B^{1\ plus\ 3}$. B^7 has merely

*From the Department of Anatomy, University of Minnesota.

shifted its position laterally. The fact that it has a common stem with B^8 is no more pertinent than that the middle lobe bronchi (B^4 and B^5) have a common stem. In fact there is more reason for considering the middle lobe a single segment.

The Right Upper and Middle Lobes

These two lobes are frequently fused, especially on the mediastinal surface. Together they may be compared to the left upper lobe, each large unit containing five segmental bronchi.

The mode of branching of the *upper lobe bronchus*[7] is prevailingly trifurcate (46 per cent of fifty specimens) but the bronchus is subdivided into B^1, B^2 and B^3 (figs. 2 and 5) in only 38 per cent. The 54 per cent of bifurcate types may be divided into four more or less equal groups—namely three in which B^1 or B^2 or B^3 (or most of each bronchus) forms one of a pair of trunks, and a fourth (the quadrivial type) in which B^3 splits into two components, the B^3a ramus arising in conjunction with B^1, and the B^3b ramus in

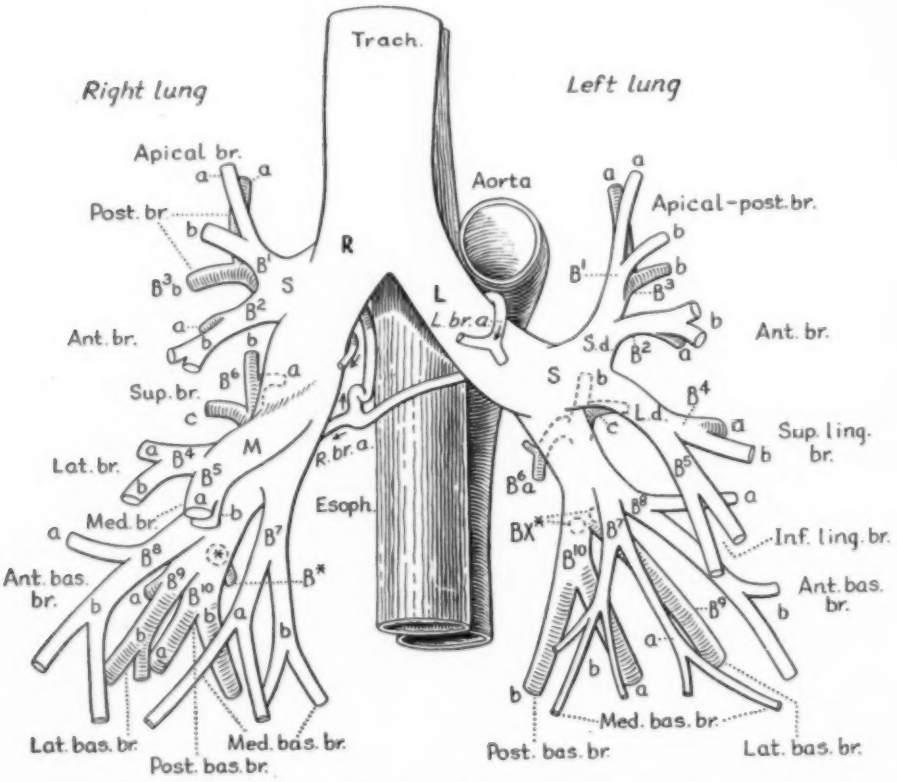


FIGURE 1: Anterior view of bronchial tree, illustrating prevailing mode of branching of segmental bronchi. (Modified from Boyden, Surgery, 1945). S., M. (of right lung), superior and middle lobe bronchi; S.d., L.d. (of left lung), superior and lingular (inferior) divisions of upper lobe bronchus; B*, BX*, subsuperior and accessory subsuperior bronchi; B^1, B^2, etc., apical and anterior segmental bronchi, etc.; a, b, their principal rami.

conjunction with B^2. Also, of special interest[7] are the 28 per cent of cases in which B^1b arises as an accessory branch (BX^1b) of B^2. In such anomalies, pus from an apical lesion could discharge through the orifice of the anterior segmental bronchus; and, of course, the size of the anterior segment would be greatly increased.[11] For rarer or less striking variations, and for patterns and variation of arteries and veins, the reader is referred to Reference 7.

A preliminary study of the *middle lobe bronchus,* based as yet on only 33 specimens,[5] suggests that the principal bronchial variation centers around the inferior ramus of the medial segmental bronchus—the one which supplies the diaphragmatic surface of the middle lobe (B^5b, figs. 2, 5 and 10). It may arise in conjunction with the lateral segmental bronchus (B^4), or as an accessory branch of it, or even as one of three bronchi into which the middle lobe stem trifurcates. Incidentally, the plane which separates medial and lateral segments is crossed more frequently by large arteries than in any other pair of adjacent segments (53 per cent of 33 specimens). For arrangement of vessels, see Reference 2.

The Left Upper Lobe

The mode of branching of the left upper lobe bronchus, in contrast to that of the right is prevailingly bifurcate. In 73 per cent of 100 specimens[4] it divides into a superior and an inferior (lingular) division. In the large remainder (27 per cent) it trifurcates into a modified upper division, an anterior bronchus (B^2) and a lower (lingular) division.[6] This is due to one of two processes—either to a downward displacement of B^2 or to a splitting of B^2 with downward displacement of its larger inferior component—the upper component remaining as an accessory anterior bronchus (BX^2) at the usual site.

This *splitting of the anterior bronchus*—i.e., its embryonic origin from two bronchial buds instead of one—is vital to an understanding of the left upper lobe. The process occurs in 33 per cent of 100 specimens.[4]

Another significant variation, frequently associated with the splitting of the anterior bronchus, is the *downward displacement of the anterior ramus of the apical bronchus* (B^1b). In 38 per cent of 100 specimens[4] it develops as an accessory ramus (BX^1b) of B^2 (or of BX^2). Such a shifting of B^1b provides a bronchial pathway (on the left side as on the right) by means of which a diseased process in the apex can involve a major portion of the lobe in an appreciable number of lungs. As a result of these two processes, the anterior segment is either greatly enlarged (11 per

cent) or reduced to at least half of its normal size (33 per cent).[10]

A third important variation[6] is the *absence of the posterior ramus of the anterior segment,* B^2a, (in 35 per cent of 100 specimens[4] and its replacement by BX^2a, an accessory ramus of the lingular division (12 per cent of specimens).[4,10] This anomalous branch and its artery constitutes an anatomical hazard to lingulectomy.[3]

A fourth variation is the deeply *cleft left upper lobe.* It has been observed in 8 per cent of 100 specimens.[4] The "middle lobes," thus formed have been classified into four types: 1) a true middle (or lingular) lobe; 2) a compressed lingular lobe; 3) an expanded lingular lobe; and 4) the ectopic arterial type associated with the occurrence of an ectopic pulmonary artery.

EXPLANATION OF FIGURES, PLATE I)

(Sketches rendered for publication by Lawrence B. Benson)

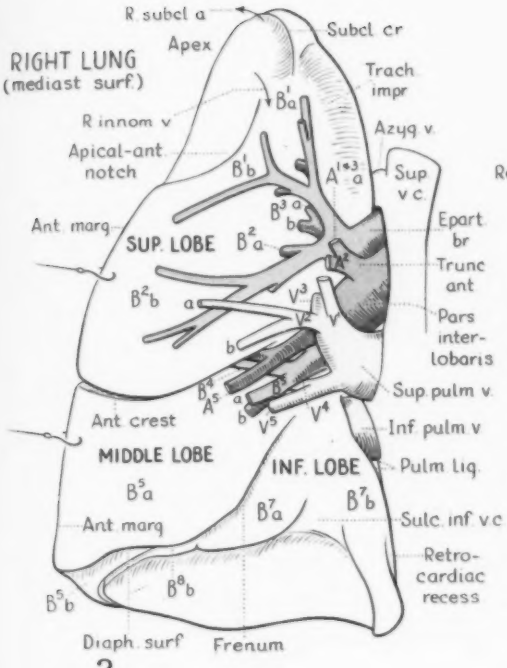
Prevailing patterns of the bronchopulmonary segments of the right upper and middle lobes, and of the left upper lobe.

SEGMENTAL BRONCHI

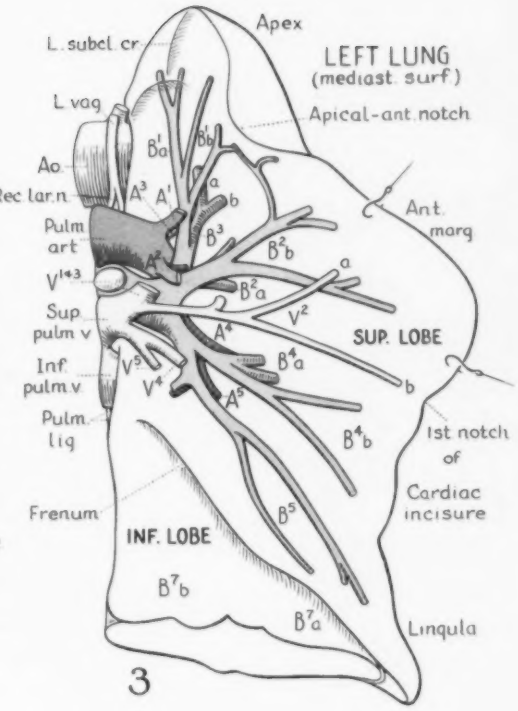
Superior lobe (Right)	*Superior division* (left superior lobe)
B^1 - *Apical bronchus*	$B^{1\ plus\ 3}$ - *Apical-posterior bronchus*
B^1a - apical ramus	B^1a, B^3a - apical rami
B^1b - anterior ramus	B^1b, B^3b - anterior and posterior rami
B^2 - *Anterior bronchus*	B^2 - *Anterior bronchus*
B^2a - posterior ramus	B^2a - posterior ramus
B^2a 1 - superior subramus	
B^2a 2 - inferior subramus	
B^2b - anterior ramus	B^2b - anterior ramus
B^3 - *Posterior bronchus*	
B^3a - apical ramus	
B^3b - posterior ramus	

Middle lobe (Right)	*Inferior (lingular) division* (Left)
B^4 - *Lateral bronchus*	B^4 - *Superior lingular bronchus*
B^4a - posterior ramus	B^4a - posterior ramus
B^4b - anterior ramus	B^4b - anterior ramus
B^5 - *Medial bronchus*	B^5 - *Inferior lingular bronchus*
B^5a - superior ramus	B^5a - superior ramus
B^5b - inferior ramus	B^5b - inferior ramus

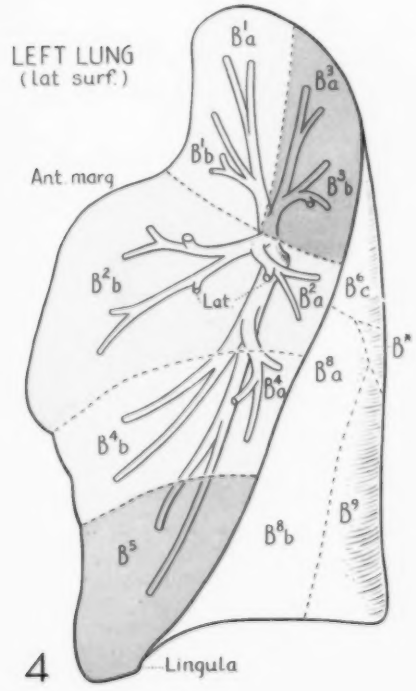
Note that in the left lung (figs. 3 and 4) the anterior segment extends along the anterior margin between the apical-anterior notch and the first notch of the cardiac incisure. In the right lung (figs. 2 and 5) it begins lower down between the first and second thirds of the anterior margin. In the right upper lobe (fig. 5) the line between the anterior and posterior segments approximates the junction between the oblique (interlobar) and horizontal (secondary) fissure, but it tends to overlap the latter. In the left upper lobe (fig. 4) three posterior rami supply the interlobar surfaces, B^3b, B^2a and B^4a. In the left apical region $B^{1\ plus\ 3}$ forms a single segment (fig. 3). Usually it divides into B^1 and B^3 to aerate separate subsegments, but frequently B^1b arises from B^2, and B^3b slides down the stem of $B^{1\ plus\ 3}$ to arise near its base. B^1a usually heads for the subclavian crest, B^1b for the apical-anterior notch (fig. 3). In the middle lobe, B^5a may be found by locating the artery (A^5a) which underlies the medial side of the anterior crest (fig. 2); B^5b runs on the inferior side of the lobe, just lateral to the frenum. Final naming of the B^4 awaits study of a larger number of specimens. At times the two rami have a superior-inferior relationship.


R subcl a
Subcl cr
Apex
RIGHT LUNG
(mediast surf.)
Trach impr
R innom v
Azyg v
Apical-ant notch
Sup v c
Ant marg
SUP. LOBE
Epart br
Trunc ant
Pars inter-lobaris
Sup pulm v
Ant crest
Inf pulm v
MIDDLE LOBE
INF. LOBE
Pulm lig
Sulc inf v c
Ant marg
Retro-cardiac recess
Diaph surf
Frenum

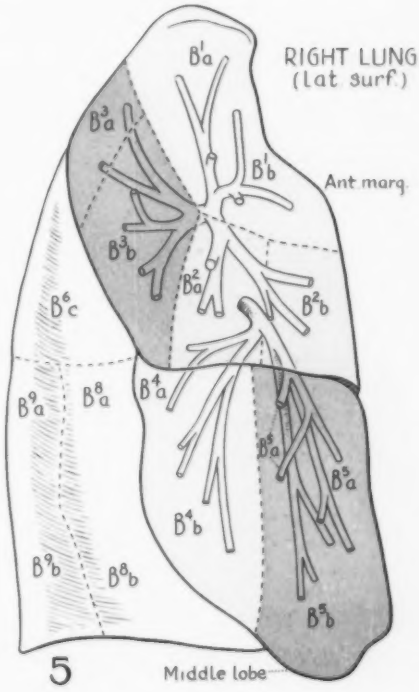
2


Apex
L subcl cr
LEFT LUNG
(mediast surf.)
L vag
Apical-ant notch
Ao
Rec lar n
Ant marg
Pulm art
SUP. LOBE
Sup pulm v
Inf pulm v
1st notch of Cardiac incisure
Pulm lig
Frenum
INF. LOBE
Linqula

3


LEFT LUNG
(lat surf.)
Ant marg
Lat
Linqula

4


RIGHT LUNG
(Lat surf.)
Ant marg
Middle lobe

5

In closing this résumé of the left upper lobe, the *variability of the apical-anterior segment* should be emphasized. Mention has already been made of the displaced B^1b. Similarly, B^3b tends to slide down the stem of B^3, so that in 36 per cent of specimens,[6] the apical-anterior bronchus divides into B^3b and $B^{1\ plus3a}$. For variations of arteries and veins the reader is referred to Reference 6.

The Right Lower Lobe

Posteriorly, the lower lobes may be divided into three transverse zones (figs. 8 and 9), namely a superior segment (B^6), a layer of basal segments ($B^{7\text{-}10}$) and an interpolated subsuperior zone which, because of the variability of its bronchial components, has been given the designation B^* (and/or BX^*).[2]

On the right side (fig. 6) the *superior segmental bronchus* bifurcates, (86 per cent of 50 specimens) into a lateral (B^6c) and superior and medial (B^6b+a) rami.[12] Because B^6a is usually a small ramus the superior segment usually caps the basal segments horizontally (62 per cent of specimens). In most of the remainder, B^6a invades the lower paravertebral surface, giving rise to an oblique capping. In such specimens it would be more difficult to resect the superior segment. Incidentally, the line between B^6c and B^8a on the anterior surface (fig. 6) usually coincides with the interfissural crest—a low ridge that separates the impressions made by upper and middle lobes. Other details of the rami of B^6 may be found in Reference 12.

The *subsuperior bronchus* (B^*) is a dorsal ramus which grows out of the stem bronchus a varying number of centimeters beneath the superior bronchus (figs. 1 and 6). Next to B^6 it is said to be most vulnerable to aspirated material. It has been found in 62 per cent of 50 specimens. Almost always it aerates the posterior sector of the costal surface above B^{10} (fig. 9), but frequently it spreads medially or laterally. When absent, as such (38 per cent), its place is taken by the accessory subsuperior (BX^*)—a high dorsal branch of B^{10}. In 48 per cent, both the subsuperior proper (B^*) and the accessory ramus $BX^*(10)$ are present in the same specimen (fig. 9). Since one or both of these occur in every specimen, the interpolated subsuperior zone is a characteristic feature of the right lower lobe.

The *basal segmental bronchi* are four in number. The medial basal (B^7 is the highest branch (fig. 1), the lateral basal (B^8) is next and then the common stem of the lateral basal and the posterior basal (B^9 and B^{10}). All of these reach the diaphragm (fig. 10).

The *medial basal segmental bronchus* (B^7) is of special interest as representing the infracardiac bronchus of mammalian quad-

rupeds, in which animals it forms a separate lobe occupying the space between the heart and diaphragm. In man, the corresponding segment is often separated from the anterior basal (36 per cent) by a supernumerary fissure of varying depth (fig. 6). The segment usually occupies the antero-medial portion of the lobe (78 per cent) being represented on both anterior and paravertebral surfaces (figs. 6 and 9). It is thus placed athwart the other basal segments (fig. 10). These segments, in turn, obliquely overlap each other. Anteriorly, the segment is grooved by the inferior vena cava. In 14 per cent of specimens the segmental bronchus (B^7) is absent as such, being represented by accessory rami of adjacent segments (B^8 or B^*). In another 8 per cent it is wholly anterior in its distribution.[12]

The *anterior basal segmental bronchus* (B^8) is remarkably con-

EXPLANATION OF FIGURES, PLATE 2

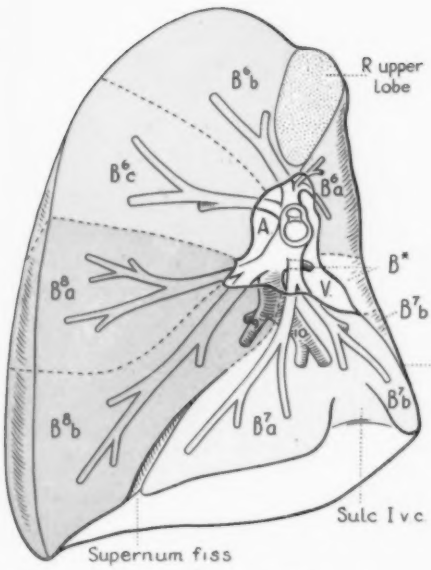
(Sketches rendered for publication by Lawrence B. Benson)

Prevailing patterns of bronchopulmonary segments of the lower lobes.

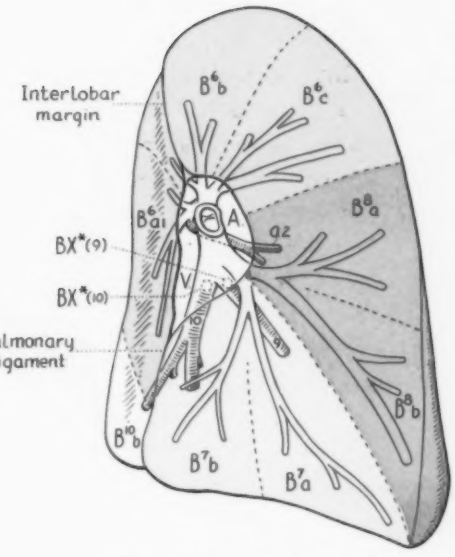
SEGMENTAL BRONCHI

Right inferior lobe	*Left inferior lobe*
B^6 - *Superior bronchus*	B^6 - *Superior bronchus*
B^6a - medial ramus	B^6a - medial ramus
	B^6a 1 - paravertebral branch
	B^6a 2 - posterior branch
B^6b - superior ramus	B^6b - superior ramus
B^6c - lateral ramus	B^6c - lateral ramus
B^* - *Subsuperior bronchus*	B^* - *Subsuperior bronchus*
BX^* (10) - accessory subsuperior bronchus	BX^* (9), BX^* (10) - accessory subsuperior bronchus
B^7 - *Medial basal bronchus*	B^7 - *Medial basal bronchus*
B^7a - anterior ramus	B^7a - lateroanterior ramus
B^7b - medial ramus	B^7b - medioanterior ramus
B^8 - *Anterior basal bronchus*	B^8 - *Anterior basal bronchus*
B^8a - lateral ramus	B^8a - lateral ramus
B^8b - basal ramus	B^8b - basal ramus
B^9 - *Lateral basal bronchus*	B^9 - *Lateral basal bronchus*
B^9a - lateral ramus	BX^* (9) - accessory subsuperior ramus
B^9b - basal ramus	B^9b - basal ramus = B^9
B^{10} - *Posterior basal bronchus*	B^{10} - *Posterior basal bronchus*
BX^* (10) - accessory subsuperior ramus	BX^* (10) - accessory subsuperior ramus
$B^{10}a$ - laterobasal ramus	$B^{10}a$ - laterobasal ramus
$B^{10}b$ - mediobasal ramus	$B^{10}b$ - mediobasal ramus

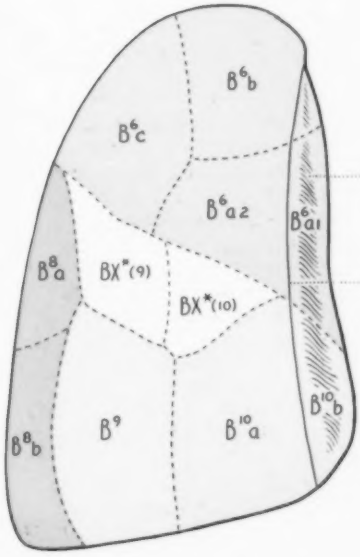
Note that on the right side (figs. 6 and 9) the superior segment caps the basal segment horizontally; on the left side (figs. 7 and 8), obliquely. Also note that B^6a on the left has a posterior branch (B^6a 2, fig. 7). On the right the subsuperior zone is prevailingly in the posterior sector of the costal surface (fig. 9) and is formed by both the subsuperior proper (B^*) and an accessory subsuperior (BX^*) from the top of B^{10}; on the left side (fig. 8) the zone lies primarily in the posterolateral sector and is usually formed by accessory subsuperiors (BX^*) from the top of B^9 and B^{10}. In only 29 per cent is there a subsuperior proper (B^*) on the left side. Finally on the right (fig. 9) B^7b extends onto the paravertebral surface. A., V., position of interlobar portion of pulmonary artery and of inferior pulmonary vein.



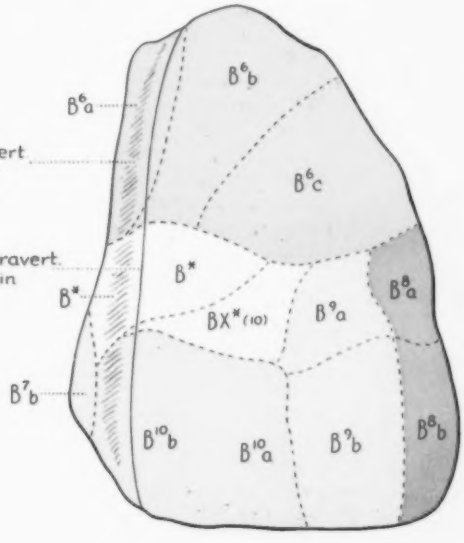
6 RIGHT LOWER LOBE
(Ant. surface)



7 LEFT LOWER LOBE
(Ant. surface)



8 LEFT LOWER LOBE
(Post. view)



9 RIGHT LOWER LOBE
(Post. view)

stant in its division into lateral and basal rami and in the distribution of its lateral ramus (B^8a, figs. 6 and 9). Its basal ramus (B^8b) is more variable in distribution since it tends to invade the basal portions of adjacent segments. Anteriorly, it occupies the lateral third of the anterior surface, as measured along the inferior margin (50 per cent of specimens; fig. 6), but when B^7 is defective it may extend to the sulcus of the inferior vena cava. In such specimens (16 per cent), B^7a develops as an accessory ramus of B^8b. Similarly, when B^9 is absent (8 per cent), B^8 takes over the diaphragmatic portion of that segment (B^9b, fig. 10). B^8, therefore is one of the dominant segmental bronchi.

By contrast, the *lateral basal segmental bronchus* (B^9) is less constant. It is smaller than the anterior basal and appears to be more like a secondary branch of the posterior basal (B^{10}, fig. 6). As noted above, it has been found absent, as such, in 8 per cent of specimens. Its lateral branch (B^9a, fig. 1) is absent in 14 per cent. Its territory is then taken over by the subsuperior (B^*) or, less commonly, by B^8a.

The *posterior basal segmental bronchus* (B^{10}) is invariably present. Its highest dorsal branch, occurring in 86 per cent of specimens, has already been demonstrated to be an accessory subsuperior and redesignated as $BX^*(10)$. The main bronchus divides into a laterobasal ($B^{10}a$) and a mediobasal ramus ($B^{10}b$). The latter is thought by some to represent the termination of the stem bronchus. It invariably heads for the inferior medial corner of the lobe (fig. 10). For arrangement of vessels, see Reference 2.

The Left Lower Lobe

Although possessing units that are comparable to those of the right side, the left lower lobe bronchus (fig. 1) presents characteristic differences in mode of branching and in the distribution of its bronchi.[1]

The prevailing pattern of the *superior segmental bronchus* (fig. 7), although bifurcate (85 per cent of 60 specimens), has the formula B^6a and B^6b+c in 43 per cent of specimens. This accentuation of its medial ramus (B^6a) has two consequences. First, because of the downward paravertebral extension of B^6a (two-thirds or more of the distance to the diaphragm in 57 per cent of specimens) the superior segment usually caps the basal segments obliquely (fig. 8). In the right lobe, it is prevailingly horizontal (62 per cent). Second, the development of a large dorsal branch in 45 per cent of specimens (B^6a 2, fig. 7) displaces the subsuperior zone to a primarily posterolateral sector on the costal surface (fig. 8).

The *subsuperior proper* (B*) is present in only 29 per cent (of 60 specimens) as contrasted with the 62 per cent of the right side. It always supplies the posterolateral sector, and may spread to the posterior or lateral sectors, but has never been found paravertebrally as on the right side. It arises a varying number of centimeters below the superior bronchus (B^6). Since it determines the characteristic location of the subsuperior zone, any other rami which supply this zone in its absence (or coordinately with it) are designated *accessory subsuperior bronchi* (BX*). These arise as high branches of the lateral basal and posterior basal bronchi—figs. 7 and 8, BX*(9) and BX*(10). The former occurs in 67 per cent, the latter in 84 per cent of 60 specimens. Since these are more numerous than the subsuperior proper (B*) the prevailing pattern of the subsuperior zone is shown in fig. 8 as being made up of the two accessory subsuperiors (43 per cent). Whatever its composition, however—whether consisting of one (22 per cent), two (61 per cent) or three components (17 per cent)—the zone is always present as a potential recipient of aspirated material, next in importance to the superior segment.

The *basal segmental bronchi* (B^{7-10}) differ from those of the right lung both in origin and in other substantial respects. The prevailing pattern of the basal trunk (omitting the subsuperiors)

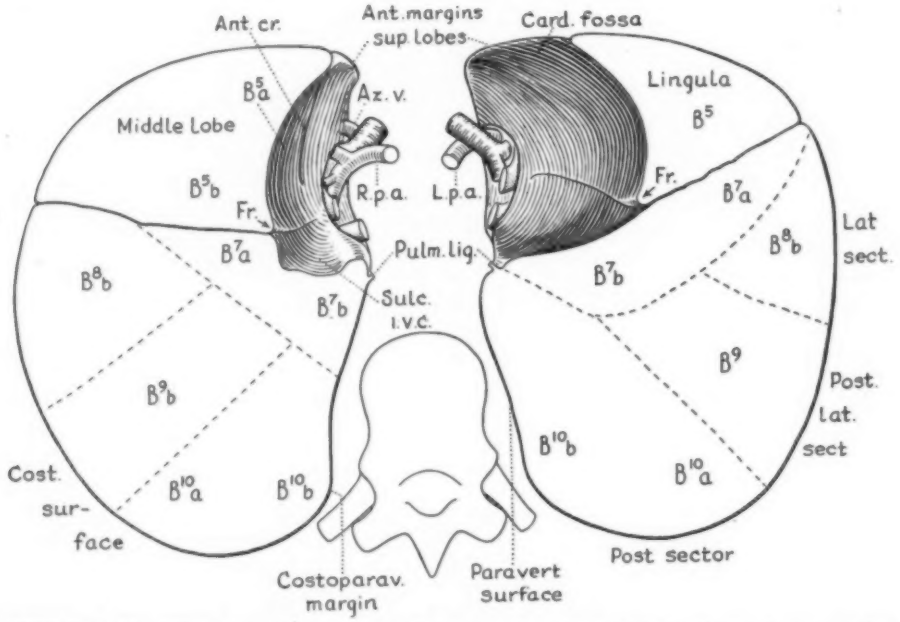


FIGURE 10: Diaphragmatic view of lungs showing distribution of segmental bronchi. (Modified, from Berg, Boyden and Smith, J. Thor. Surg., 1949). *Ant. cr.*, anterior crest of middle lobe rising up to anterior margin; *Az. v.*, azygos vein; *Fr.*, frenum of middle lobe or of left upper lobe; *R.p.a., L.p.a.*, pulmonary arteries; *Sulc. i.v.c.*, groove in the anterior surface of the right lower lobe made by the inferior vena cava.

is a bifurcation (87 per cent). Most commonly (67 per cent) the trunk divides into $B^{7\ plus\ 8}$ and $B^{9\ plus\ 10}$ (fig. 7).

The *medial basal segmental bronchus* (B^7) has shifted laterally, so that in 87 per cent it arises in common with B^8 or one of its rami. (In 10 per cent it arises independently, as on the right side, and in 3 per cent it is absent, as such). Correspondingly the segment which it aerates has shifted laterally, so that prevailingly (55 per cent) it occupies the whole of the inferior anterior surface of the lobe (fig. 7). B^{10} takes over the paravertebral territory vacated by this shift (fig. 10). In 20 per cent, B^7 may supply only the medial half to two-thirds of the lower anterior surface and in 22 per cent it may invade the anterior costal territory of B^8.

The *anterior basal segmental bronchus* (B^8) is far from being the dominant segment that it is on the right side. In 70 per cent, it arises in common with B^7, and in 13 per cent it arises independently. In the remaining 17 per cent, either its basal or lateral ramus is absent, as such; in these instances B^8a is taken over by an accessory branch of the subsuperiors, and B^8b by an accessory ramus of 8^7 or B^9. In a different 17 per cent the basal ramus fails to reach the diaphragm. Prevailingly, the distribution is that shown in fig. 7, but in 27 per cent it encroaches upon B^7a and in 17 per cent it is crowded out of the diaphragmatic and lateral costal area.

The *lateral basal segmental bronchus* (B^9) occupies the posterior lateral sector of the lobe as on the right side (fig. 10), with the exception that its high lateral branch (present in 67 per cent of specimens) supplies the subsuperior zone and hence has been designated BX*(9). B^9 is absent, as such, in 10 per cent of specimens, its territory being taken over usually by an accessory branch of B^7.

The *posterior basal segmental bronchus* (B^{10}) is much like that of the right lung except that it takes over the paravertebral zone of B^7b (figs. 8 and 10), and in 30 per cent of specimens a high paravertebral branch is given off before B^{10} divides into its laterobasal and mediobasal rami. For arrangement of vessels, see Reference 2.

DISCUSSION

In concluding this brief résumé of the bronchopulmonary segments, the writer feels that it would be useful to discuss the way in which the above observations differ from those of Brock (1942-44) and of Jackson and Huber (1943)—the two systems which deservedly have obtained greatest recognition in the British Empire and in this country.

Aside from the fact that our articles have included a descrip-

tion of segmental arteries, veins and of subsegments, the three series of publications seem to be in general agreement. It is obvious that all three are dealing with the same major branches of the bronchial tree—a statement which does not always apply to older or more recent continental studies.

Jackson and Huber, without publishing the data on which their observations rest, have presented what might be termed the "normal arrangement" of the bronchopulmonary segments, using a terminology of directional terms which is consistent with the Basel Anatomical Nomenclature. While accepting the terms, we would suggest the following minor changes in the disposition of segments. Prevailingly, on the right, the medial basal segment (B^7) lies on both sides of the pulmonary ligament. On the left, the anterior segment (B^2) borders on the interlobar fissure. In the left lower lobe, the anterior-medial basal segment should be separated into its two components, B^7 and B^8, making a total of nine segments in the left lung. Finally, we feel that it is desirable to recognize a more or less constant subsuperior zone in each lower lobe, even though it cannot be considered to be a segment because of its variable composition.

To Brock we are indebted for an extraordinarily clear, comprehensive and significant account of the anatomy of the bronchial tree. He has related the segments to the thoracic wall, and casts of the tree to bronchographic appearances; he has stressed the importance of "axillary" rami (first noted by Lucien and Weber) and recorded numerous variations in the extent of the segments. We feel that our work began where Brock left off. By going one step further, i.e. by identifying both the segmental and subsegmental bronchi on the basis of their prevailing distribution and not merely by their origin on the tree, we have obtained an additional tool for interpreting variations. For example, in specimens in which the upper division of the left upper lobe bronchus has only two branches—the lower of which supplies the upper anterior zone (Brock's fig. 50), and the upper of which supplies the apex and the posterior zone—Brock is obliged to call the lower one "apical" and the upper one "subapical." By analyzing the subsegments we can more accurately describe the lower branch as an "accessory anterior" and the upper branch as the apical-posterior bronchus ($B^{1\ plus\ 3}$).

In other words, we have applied to the human lung Huntington's concept that the lungs of higher vertebrates are plastic organs and that the primary cause of variations is the opportunistic tendency of bronchial buds to grow into a given zone from more than one point on the embryonic tree. The key to such variations is thus the displacement of rami.

DISCUSION

Como conclusión de este breve resumen de los segmentos broncopulmonares, el autor cree que sería útil discutir la forma en que las observaciones que anteceden difieren de las de Brock (1942-44) y de Jackson y Huber (1943), los dos sistemas que merecidamente han obtenido mayor aceptación en el Imperio Británico y en éste País.

Fuera del hecho de que nuestros artículos han incluído una descripción de las arterias y venas segmentarias, las tres series de publicaciones parecen en general estar de acuerdo. Es evidente que las tres se refieren a las mismas ramas mayores del árbol bronquial, afirmación que no siempre puede aplicarse a estudios más antiguos o más recientes en Europa.

Jackson y Huber, sin publicar los datos en que se basan sus observaciones, han presentado lo que podría llamarse la "forma normal" de los segmentos broncopulmonares usando una terminología direccional de acuerdo con la Nomenclatura Anatómica de Basilea. Aunque aceptamos los términos sugeriríamos los siguientes cambios menores en la disposición de los segmentos. Predominantemente, en el lado derecho, el segmento medio basal (B^7) se encuentra a ambos lados del ligamento pulmonar. A la izquierda, el segmento anterior (B^2) limita con la fisura interlobar.

En el lóbulo inferior izquierdo el segmento basal antero-medio debe ser disgregado en dos componentes: B^7 y B^8, lo que hace un total de nueve segmentos en el pulmón izquierdo. Por último creemos que es desearse que se reconozca una zona subsuperior más o menos constante, aunque no pueda considerarse como un segmento a causa de su composición variable.

Debemos a Brock una descripción extraordinariamente clara y comprensiva de la anatomía del árbol bronquial. Ha relacionado los segmentos a la pared torácica y las proyecciones del árbol a los aspectos broncográficos; ha insistido sobre la importancia de las ramas "axilares" (primero señaladas por Lucien y Weber) y ha referido numerosas variantes en la extensión de los segmentos. Creemos que nuestro trabajo empezó donde Brock lo dejó. Yendo más adelante, o sea identificando tanto los bronquios segmentarios como los subsegmentarios basándonos en su predominante distribución y no solamente en su origen troncal, hemos obtenido un recurso adicional para interpretar las variaciones. Por ejemplo en los especímenes en los que la división superior del bronquio del lóbulo superior izquierdo tiene solo dos ramas—la inferior de las cuales corresponde a la zona superior anterior (Brock, Fig. 50) y la superior de la cual corresponde al vértice y

la zona posterior—Brock se ve obligado a llamar la más baja "apical" y la superior "subapical."

Analizando los subsegmentos podemos con más exactitud describir la rama inferior como una "accesoria anterior" y la superior como el bronquio apical anterior ($B^{1 \text{ plus } 3}$).

En otras palabras, hemos aplicado al pulmón humano el concepto de Huntington de que los pulmones de los vertebrados superiores son órganos plásticos y que la causa primaria de las variaciones es la tendencia oportunista de las yemas bronquiales a crecer dentro de una zona determinada desde más de un punto de origen en el árbol embrionario. La clave de tales variaciones es así la presencia de bronquios accesorios o desplazados.

REFERENCES

1 Berg, Roger M., Boyden, Edward A. and Smith, Franklin R.: "An Analysis of Variations of the Segmental Bronchi of the Left Lower Lobe of Fifty Dissected, and Ten Injected, Lungs," *J. Thor. Surg.*, (April) 1949.*

2 Boyden, Edward A.: "The Intrahilar and Related Segmental Anatomy of the Lung," *Surgery*, 18:706-731, 1945.

3 Boyden, E. A.: "The Anatomical Hazards of Lingulectomy," *Surgery*, 20:828-829, 1946.

4 Boyden, Edward A.: "Cleft Left Upper Lobes and the Split Anterior Bronchus," *Surgery*, (in press), 1949.

5 Boyden, Edward A. and Christopher J. Hamre: "Preliminary Observations on the Pattern of the Middle Lobe of the Right Lung," *Anat. Rec.*, 103, (March) 1949.*

6 Boyden, Edward A. and Hartmann, J. Francis: "An Analysis of Variations in the Bronchopulmonary Segments of the Left Upper Lobes of Fifty Lungs," *Am. J. Anat.*, 79:321-360, 1946.

7 Boyden, Edward A. and Scannell, J. Gordon: "An Analysis of Variations in the Bronchovascular Pattern of the Right Upper Lobe of Fifty Lungs," *Am. J. Anat.*, 82:27-74, 1948.

8 Brock, R. C.: "Observations on the Anatomy of the Bronchial Tree, with Special Reference to the Surgery of Lung Abscess," *Guy's Hospital Reports*, 91:111-130; 92:26-37, 82-88 and 123-144; 93:90-107, 1942-44. (Also Oxford Univ. Press, 1946).*

9 Jackson, Chevalier L. and Huber, John Franklin: "Correlated Applied Anatomy of the Bronchial Tree and Lungs with a System of Nomenclature," *Dis. of Chest*, 9:1-9, 1943.*

10 Scannell, J. Gordon: "A Study of Variations of the Bronchopulmonary Segments in the Left Upper Lobe," *J. Thor. Surg.*, 16:530, 1947.*

11 Scannell, J. G. and Boyden, E. A.: "A Study of Variations of the Bronchopulmonary Segments of the Right Upper Lobe," *J. Thor. Surg.*, 17:232-237, 1948.*

12 Smith, Franklin R. and Boyden, Edward A.: "An Analysis of Variations of the Segmental Bronchi of the Right Lower Lobe of Fifty Injected Lungs," *J. Thor. Surg.*, (April) 1949.*

*Articles marked with an asterisk are based in part upon injection of fresh specimens.

Surgical Treatment of Emphysematous Blebs and Bullae*

O. THERON CLAGETT, M.D.**
Rochester, Minnesota

The first report in medical literature dealing with the subject of cystic disease of the lung is probably that of Thomas Bartholinus[1] found in the Leyden edition of Malpighius in 1687. By 1925 Koontz[2] was able to collect 108 cases in the literature, reported, for the most part, in German medical journals. With the development of thoracic surgery and the widespread use of roentgenologic examination of the thorax, interest in this condition has grown steadily. By 1936 Schenck[3] was able to report a series of 381 cases collected from the literature and during the last ten years many additional cases have been reported, particularly in American and British journals. It has become apparent that cystic disease of the lung is not a rare disease. All physicians and surgeons interested in thoracic disease have become familiar with this condition.

There is still considerable difference of opinion regarding the proper classification of the various lesions included in cystic disease of the lung, the genesis of these lesions, whether congenital or acquired, and the terms that should be used to describe these lesions. It is generally agreed, however, that cystic lesions of the lung can be divided into two chief types: those that originate from the bronchial tree and those that are alveolar in origin.

Bronchiogenic cysts are characterized by the fact that they possess an epithelial lining of cuboidal or columnar cells which may be smooth and regular, or roughened and trabeculated. Bronchiogenic cysts may contain fluid, pus, blood or air alone or in combination. Most of the literature on cystic disease of the lung has been concerned with these cysts of bronchial origin. Their clinical and roentgenologic manifestations are well known. It is universally agreed that they can be treated best by surgical excision.

Very little consideration has been given in medical literature to the cystic lesions of the lung of alveolar origin, which include pulmonary blebs, bullae and pneumatoceles. Apparently these lesions are not as well understood as the more common cysts of

*Presented at the 14th Annual Meeting of the American College of Chest Physicians, Chicago, Illinois, June 18, 1948.
**Division of Surgery, Mayo Clinic, Rochester, Minnesota.

bronchial origin and the possibility of benefiting patients with these lesions by surgical means is not appreciated generally. The remainder of this discussion will be devoted to these cysts and their surgical management.

A pulmonary bleb is a localized air pocket situated immediately beneath the parietal pleura. According to Miller,[4] a bleb results from rupture of the subserous layer of connective tissue of the pleura by air from ruptured alveoli separating the pleura proper from the underlying pulmonary tissue. The air extends along tissue planes much as a dissecting aneurysm extends along the wall of an artery.

Bullae and pneumatoceles are located primarily deeper in the lung than are blebs. Maier[5] has defined a pneumatocele as a hyperinflated intrapulmonary cavity produced by the marked distention of a defect in the pulmonary parenchyma. Bullae are believed to result from rupture of dilated alveoli into one another and their coalescence to form intrapulmonary air pockets. I doubt if there is much if any difference between bullae and pneumatoceles. Certainly they cannot be differentiated clinically or roentgenologically, and in the remainder of this discussion I shall use only the terms "blebs" and "bullae." Pulmonary blebs and bullae may be single or multiple. They may involve a single lobe or any combination of lobes. They may occur as a part of a generalized pulmonary emphysema or may occur in any part of a lung in the absence of any detectable evidence of emphysema. They can occur at any age.

The genesis of isolated blebs or bullae in the absence of generalized emphysema is not completely clear. Naclerio and Langer[6] have expressed the belief that they are usually of congenital origin. Undoubtedly in some cases they do originate in this way. However, it is my opinion that localized inflammatory processes involving small bronchi and bronchioles may result in scarring and constriction of these air ducts in such a way that egress of air from the portion of the lung distal to such constriction is interfered with more than the intake of air through the constriction. This process leads to overinflation of the segment of lung involved, rupture of alveolar walls and the development of an air-containing cavity. In other words, localized inflammatory changes may produce changes in the tiny air duct which result in a valvular mechanism in the bronchi. Hayashi[7] has reported finding such valve-like structures on microscopic examination of bronchi leading into pulmonary blebs and bullae, and Allison[8] has recently reported a case in which he was able to demonstrate clearly a valvular action in the bronchus leading to a large air cyst. Allison has also pointed out that bullous cysts may arise

from some overexertion, such as coughing or straining, in the presence of an inflamed or ulcerated bronchus so that rupture of the bronchus occurs at some weak point with escape of air into the interstitial tissues of the lung. For this reason he pointed out that it is not surprising to find bullous cysts in association with bronchiectasis. Freedman[9] has expressed the belief that obstructive processes of the trachea or bronchus, whether due to intrinsic or to extrinsic lesions, may lead to the development of blebs and bullae even in the absence of generalized emphysema. He has also pointed out that air vesicles can result from the presence of foreign bodies and mucinous or pseudomucinous plugs of exudate in the bronchi as well as scarred, constricting lesions of the bronchus.

The chief symptom caused by pulmonary blebs and bullae is dyspnea. They may also produce pain, usually pleuritic in character; and they may become infected, with the development of the usual picture of an infected pulmonary cyst. Cough is not a prominent symptom. The dyspnea in most cases which occurs in patients with blebs and bullae may be of gradual onset and progression as the cysts enlarge, destroying the adjacent pulmonary parenchyma and compressing the remainder of the lung. If the process is extensive enough a patient may even die of asphyxia because of insufficient functioning pulmonary tissue to maintain the respiratory requirements.

Perhaps the commonest manifestation of pulmonary blebs and bullae is the sudden development of dyspnea due to spontaneous pneumothorax. As these blebs and bullae gradually increase in size they reach a point at which their thin walls can no longer withstand the pressure and they rupture into the pleural space, resulting in a completely collapsed lung. Fortunately, high pressure tension pneumothorax with marked shift of the mediastinum does not develop in most cases and if it does occur it comes on gradually over a period of several days. Failure of tension pneumothorax to develop or its slow development can be accounted for by the fact that the bronchial leak is very small in these cases and tension develops slowly or the leak may be closed off when the lung collapses. In the great majority of cases of spontaneous pneumothorax the leak will seal over and the lung will re-expand gradually without any treatment. Roentgenograms of the re-expanded lung often do not show any detectable abnormality of the lung to account for the pneumothorax.

Perhaps a word should be inserted here regarding the etiology of spontaneous pneumothorax. It was once believed that this condition almost invariably resulted from pulmonary tuberculosis. It is now clearly recognized that this is not true and it seems

likely that most instances of spontaneous pneumothorax are due to rupture of pulmonary blebs and bullae. Leach[10] has reported a series of 126 cases of spontaneous pneumothorax in air force personnel. All of the patients had had negative thoracic roentgenograms previous to the development of the pneumothorax. On follow-up in none of the cases could the pneumothorax be proved to be due to tuberculosis. Kjaergaard[11] followed 51 patients who had spontaneous pneumothorax and found that in only 1 did evidence of pulmonary tuberculosis develop subsequently. There can be little question that tuberculosis is only rarely an etiologic factor in cases of spontaneous pneumothorax. In most the lesion is undoubtedly due to rupture of pulmonary blebs and bullae.

The treatment of pulmonary blebs and bullae depends necessarily on many factors. If the air-containing cavities are multiple and involve both lungs or are a part of a generalized pulmonary emphysema, little can be done for the relief of the patient. Small cysts not causing symptoms do not necessarily require any treatment. However, the patient should be warned of the potential dangers of such lesions and should be checked frequently by means of thoracic roentgenograms. Progressive increase in size warrants consideration of surgical excision if the cyst is solitary or if multiple cysts involve a single lobe or lung. Obviously, development of infection in such cysts demands surgical treatment. Fortunately, infection does not occur commonly in these lesions. Severe dyspnea due to the size of the cyst or due to the development of pneumothorax most frequently demands corrective surgical treatment. Needle aspiration of blebs and bullae is definitely contraindicated because it can result only in rupture of the cavity and the production of pneumothorax. However, in very large cystic lesions it may be impossible by roentgenologic study to ascertain without question whether the patient has a pneumothorax or a cyst so large that the collapsed lung cannot be identified. In instances of severe dyspnea due to a large cystic lesion or a tension pneumothorax it may be necessary as a life-saving measure to insert a needle to aspirate air from the involved pleural space.

In instances of spontaneous pneumothorax which from the history appear to be of recent origin, it is the practice of my colleagues and me to observe these patients for several days provided they are not acutely dyspneic in order that the leak in the lung may have an opportunity during the collapsed phase to seal over. The lung may gradually expand without intervention. If the lung does not begin to re-expand we insert a blunt needle into the pleural space, leave it in place and maintain constant

controlled gentle negative pressure to encourage re-expansion. The needle may be left in place for twenty-four to forty-eight hours, depending on the re-expansion of the lung. If the lung re-expands completely the needle is removed and the condition of the lung is followed by means of daily roentgenograms to be sure that the lung remains expanded and to see if any lesion can be demonstrated that could account for the development of the pneumothorax. If the lung does not re-expand or if after re-expansion it collapses again after removal of the needle, it is assumed that the leak will not close with conservative measures and exploratory thoracotomy is recommended, provided the patient's general condition and particularly the condition of the other lung will permit such an operation. The extent of the surgical procedure that may be necessary varies considerably. Simple repair of a small surface defect has sufficed in some instances; in others lobectomy or segmental resection of a portion of a lobe has been necessary. Rarely, pneumonectomy has been required.

Allison has suggested phrenic nerve interruption as a means of relieving the dyspnea found in some instances of bullous cysts. I have not had occasion to use this procedure as yet but it may have considerable merit. The rationale of this procedure is based on the Hering-Breuer[12] theory of the nervous control of respiration. According to this theory the limits of inspiration and expiration are regulated by the tension within the lung structure and proprioceptive impulses from the lungs, though the vagus nerves play a part in regulating the depth of respiration. If the tension within the lungs is not uniform as in the case of hyperinflated bullous lesions it is conceivable that nervous influences from this portion of lung under the greatest tension could act as a governor and limit the depth of respiration and thus cause dyspnea. Allison has reported 2 cases in which he carried out phrenic nerve interruption, reasoning that the procedure would tend to reduce inflation of the cystic lesion and hence minimize the nervous limitation of the depth of respiration. One patient was relieved of his dyspnea for four months. The dyspnea returned with the return of diaphragmatic motion and was again relieved when the phrenic nerve on the involved side was permanently interrupted. In a second case the vital capacity was 1,700 ml. before phrenic nerve interruption and 2,600 ml. after interruption, and the dyspnea was relieved. Head[13] has treated some bullous lesions of the lung by Manaldi suction. We have not had experience with this method.

The following cases represent examples of emphysematous blebs and bullae and the various surgical procedures that were used in their treatment.

Figure 1 a: Complete collapse of the left lung with tension pneumothorax on the left and mediastinal hernia.—*Figure 1 b:* Blunt needle in left thoracic cavity connected to continuous suction device. The lung is only partially re-expanded. The mediastinal hernia has been reduced about half.—*Figure 1 c:* Almost complete re-expansion of the lung after surgical repair of the bronchopleural fistula.

REPORT OF CASES

Case 1: A white woman, 28 years of age, registered at the Mayo Clinic on December 30, 1947. She stated that in October, 1944 when she was four months pregnant, there had developed chills, fever and cough accompanied by rather severe pain in the region of the left costal margin. Thoracentesis had been done but no fluid was obtained. Apparently no roentgenogram had been taken. Shortly thereafter she had a miscarriage. She continued to have marked dyspnea and a dry nonproductive cough and was sent to a sanatorium. In December, 1944 roentgenograms revealed a completely collapsed left lung. The results of all studies for tuberculosis were negative. Thoracentesis had been carried out three times, resulting in partial re-expansion of the lung. No fluid was obtained. In September, 1945 and July, 1946 roentgenograms were said to show partial collapse of the left lung. In May, 1947 the dyspnea became more marked. Aspiration of air from the chest on three occasions gave temporary relief.

On examination at the clinic the patient was found to weigh only 96 pounds (about 43 kg.). She was markedly dyspneic. The trachea was shifted to the right. There was marked hyperresonance over the left side of the chest. Roentgenograms revealed complete collapse of the left lung and tension pneumothorax (Fig. 1a). A blunt needle was inserted into the pleural space and continuous negative pressure was instituted (Fig. 1b). There was partial re-expansion of the lung. On January 6, 1948 exploratory thoracotomy was performed. The patient had a huge emphysematous bleb arising from the anterior surface of the left upper lobe. It was so large that it was attached to the diaphragm, the lateral chest wall and the apex of the chest. It had ruptured, resulting in a tension pneumothorax. In its base there were several small open bronchial fistulas. The cyst was resected and the defect in the surface of the lung was repaired. Positive pressure was applied by the anesthetist and the collapsed lung expanded readily (Fig. 1c). The postoperative course was uneventful. The patient was completely relieved of her dyspnea. She was dismissed from the hospital ten days after operation.

Case 2: An infant, five weeks of age, was registered at the clinic on August 19, 1946. The child had been born about five weeks prematurely. The pregnancy and labor had been essentially normal. From birth the child had presented a feeding problem. Breast and bottle feeding had both been attempted but had seemed to exhaust the infant. Feedings were taken slowly and were accompanied by marked dyspnea but no cyanosis or choking was noted. There had been a loss of about 1 pound (0.5 kg.) since birth despite some attempts at tube feeding. On admission the infant weighed 3,000 gm. The child was markedly dyspneic even after being placed in oxygen. Roentgenograms of the thorax revealed a large emphysematous bulla on the left with marked depression of the diaphragm and a shift of the mediastinum to the right (Fig. 2a). Exploratory thoracotomy was carried out as an emergency procedure. At operation the entire left side of the thorax was found to be filled by a huge bullous lesion arising from the lingula of the left upper lobe. The remainder of the lung appeared normal. The lingula was resected. The lower lobe and the remaining upper lobes then expanded normally, filling the left side of the thorax (Fig. 2b). The postoperative course was complicated by the development of a small empyema which healed

rapidly. The infant was dismissed on September 28, 1946. A thoracic roentgenogram on December 11, 1946 was essentially normal. The child was growing normally.

Case 3: A white man, aged 41 years, registered at the clinic on February 20, 1948. He gave a history of dyspnea on exertion for six years. This dyspnea had gradually progressed and had been quite severe the past two years. Three days before admission, after a bad coughing spell, he had become acutely dyspneic and was hardly able to walk. Physical examination indicated complete pneumothorax on the left with some shift of the mediastinum to the right. Roentgenograms confirmed this

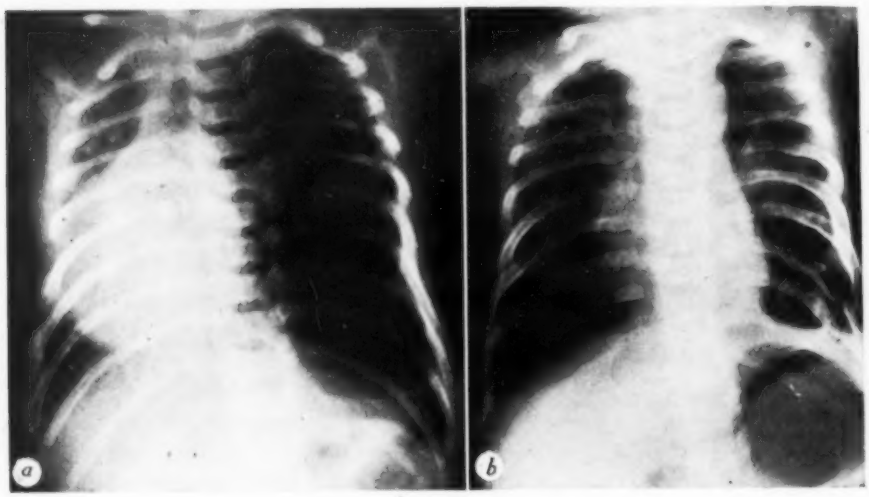


Figure 2 a: Large emphysematous bulla on the left which has depressed the diaphragm and pushed the mediastinum to the right.—*Figure 2 b:* After lingulectomy the mediastinum is in the midline, the diaphragm is in its normal position and aeration of both lungs is approximately equal.

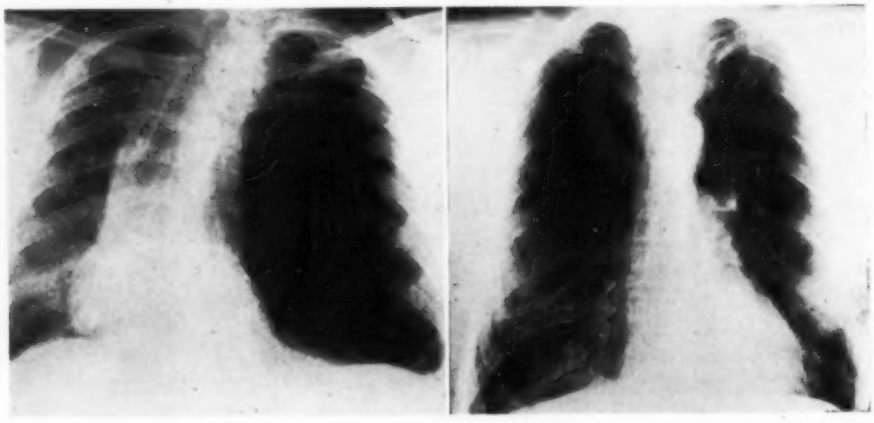


FIGURE 3 FIGURE 4

Figure 3: Tension pneumothorax on the left with marked shift of the mediastinum to the right and mediastinal hernia.—*Figure 4:* Large emphysematous bulla in the upper right portion of the thorax. Right middle and lower lobes are compressed.

diagnosis (Fig. 3). A blunt needle was inserted into the pleural space and left in place. Continuous negative pressure was maintained. The mediastinum shifted to the normal position and the left lung partially re-expanded. The patient's dyspnea was relieved. He reported that his respiration was easier than it had been for several years. After forty-eight hours the needle was removed. The lung promptly collapsed again. Exploratory thoracotomy was advised and was performed on March 2, 1948. On exploration it was found that there were many large emphysematous blebs and bullae involving the entire lung. One had ruptured and with positive pressure applied to the lung by the anesthetist the leaking bronchus could be identified. Because of the almost total destruction of functioning pulmonary tissue it was necessary to perform pneumonectomy. The postoperative course was uneventful. The patient was dismissed in good condition three weeks after operation. He reported that he had much less dyspnea than he had had before operation.

Case 4: A white man, aged 41 years, registered at the clinic on March 8, 1948. According to his history, a thoracic roentgenogram in 1939 had revealed the presence of pneumothorax on the right. The patient had not had symptoms referable to his chest until 1944 when he noted dyspnea on exertion. This gradually progressed until it had partially incapacitated him. There was little cough. The patient had never had asthma. The results of physical examination were essentially negative. The results of laboratory studies were negative except for the thoracic roentgenogram which revealed a large bulla involving the right upper lobe and markedly compressing the right lower and middle lobes (Fig. 4). The results of bronchoscopy were negative. On March 25, 1948 the right side of the thorax was explored. The pleural space was almost completely filled with multiple large bullae. The entire right upper lobe was destroyed by the lesions. There were a few small superficial bullae of the right lower lobe. The right lower and middle lobes were compressed by the bullous lesions. Right upper lobectomy was performed. The pathologist reported large emphysematous bullae of the upper lobe. No bronchial communication could be demonstrated. The postoperative course was satisfactory and the patient was considerably relieved of his dyspnea.

Case 5: The patient was a white woman, 38 years of age. On December 26, 1947 she was awakened at night with acute dyspnea. She had not had wheezing or cough previously. There was no pain. Dyspnea on the slightest exertion continued and the next day roentgenograms revealed a tension pneumothorax on the right. The dyspnea gradually improved slightly. Aspiration of air on one occasion gave slight temporary relief. Successive roentgenograms did not reveal any re-expansion of the lung. The patient came to the clinic two months after the onset of her difficulty. The lung was still completely collapsed (Fig. 5a). A blunt needle was inserted and continuous negative pressure was instituted. Partial re-expansion of the lung occurred (Fig. 5b) but the lung collapsed again when the needle was removed. The results of bronchoscopy were negative. Thoracoscopy wasd one. A bullous lesion could be seen on the surface of the upper lobe. On March 10, 1948 exploratory thoracotomy was performed. There were several hundred cubic centimeters of clear fluid in the pleural space. The lung was encased in a fibrinous membrane which prevented complete expansion of the lower lobes. There were

Figure 5 a: Complete collapse of the right lung and some depression of the right side of the diaphragm caused by tension pneumothorax. *Figure 5 b:* Blunt needle in pleural space connected to continuous suction apparatus. There is partial re-expansion of the lung.—*Figure 5 c:* Appearance after right upper lobectomy and decortication of right middle and lower lobes. The lung is expanded. Residual pneumothorax is no longer under tension.

multiple emphysematous blebs on the surface of the upper lobe. One had ruptured and there was an open bronchial fistula. The right upper lobe was resected and decortication of the right middle and lower lobes was carried out. The postoperative course was satisfactory. The remaining lobes satisfactorily filled the pleural space (Fig. 5c).

SUMMARY

The preceding cases are examples chosen from a number of similar cases that have come to my attention in recent years. As indicated, it was possible in some cases to obtain a satisfactory result by simple repair of a small surface defect; in others segmental resection, lobectomy or pneumonectomy was necessary. Before exploratory thoracotomy was performed, it was not possible in any case to determine the extent of operation that would be necessary. Since in some cases extensive pulmonary resection, even total pneumonectomy, is required, it is, of course, important to determine as accurately as possible the status of the opposite lung. The fact that these patients have been maintaining respiratory requirements with one lung, even in the presence of tension pneumothorax on the opposite side, is quite good evidence of the condition of the functioning lung. However, in some cases there may be blebs or bullae in the better lung. The most conservative surgical procedure possible should always be chosen since there is always some likelihood that the factors that have led to the development of the lesion for which operation is being performed may lead to the development of other blebs and bullae in the future. So far as we know at present this has not occurred in any of our patients as yet but the possibility must be recognized and as much functioning pulmonary tissue should be preserved as is possible under the circumstances of the individual case.

It is an interesting fact to me that these patients can have a huge air-filled cavity with bronchial communication and yet so rarely become infected. It is amazing that some of our patients have apparently gone three or four years with a complete and even a tension pneumothorax with open bronchial communication without development of a pleural infection. In some cases there may be a little clear pleural fluid; in others, none. In some instances it has been necessary to decorticate the lung before it would expand satisfactorily. In others re-expansion occurred readily when the defect was closed or the involved segment of lung was removed.

Pulmonary cysts of alveolar origin occur fairly commonly. They deserve more attention than they have received. They are not necessarily a part of a generalized pulmonary disease. They are the most frequent cause of spontaneous pneumothorax. In many instances they are amenable to corrective surgical measures with great benefit to the patient.

RESUMEN

Los casos que se han presentado representan ejemplos seleccionados de un número de casos semejantes que he tenido la oportunidad de observar en años recientes. Como se ha indicado, en algunos casos fue posible obtener un resultado satisfactorio con un reparo sencillo de un pequeño defecto en la superficie; en otros fue necesaria la resección segmentaria, la lobectomía o la neumonectomía. Antes de que se llevara a cabo la toracotomía exploratoria, no fue posible determinar en ningún caso lo extenso de la operación que sería necesaria. Ya que en muchos casos es necesario ejecutar una resección pulmonar extensa, aún una neumonectomía total, es importante que se determine, tan exactamente como lo sea posible, el estado del pulmón opuesto. El hecho de que estos pacientes han mantenidos los requisitos respiratorios con un solo pulmón, aún cuando ha existido un neumotórax hipertensivo en el lado opuesto, es muy buena prueba del estado del pulmón funcionante. Sin embargo, en algunos casos pueden existir ampollas o vejigas en el mejor pulmón. Por consiguiente, siempre se debe escoger el procedimiento quirúrgico más conservador que sea posible, pues siempre existe la posibilidad de que los factores que han conducido al desarrollo de la lesión por la cual se lleva a cabo la operación, puedan conducir en el futuro al desarrollo de otras ampollas y vejigas. Por lo que sepamos al presente, no ha sucedido esto todavía en ninguno de nuestros pacientes, pero débese reconocer la posibilidad y se debe conservar tanto tejido pulmonar funcionante como sea posible, dadas las circunstancias del caso individual.

Me parece a mí un hecho interesante que estos pacientes puedan tener una enorme cavidad llena de aire y con comunicación bronquial que, sin embargo, raramente se infecta. Es sorprendente que, aparentemente, algunos de nuestros pacientes han tenido un neumotórax completo, y aún hipertensivo, con una comunicación bronquial abierta por tres o cuatro años sin que resultara una infección pleural. En algunos casos puede existir una pequeña cantidad de derrame pleural claro; en otros, nada. En algunos casos ha sido necesario descortezar el pulmón para que se pudiera inflar satisfactoriamente. En otros, la reexpansión ocurrió fácilmente cuando se cerró el defecto o se extirpó el segmento pulmonar invadido.

Los quistes pulmonares de origen alveolar ocurren con bastante frecuencia y merecen más atención de la que han recibido. No son siempre parte de una enfermedad pulmonar generalizada. Son la causa más común del neumotórax espontáneo. En muchos casos responden a medidas quirúrgicas correctivas con gran beneficio para el paciente.

REFERENCES

1 Bartholinus, T.: Quoted by Oughterson, A. W. and Taffel, Max: "Pulmonary Cysts; Review of the Subject, with a Case Report," *Yale J. Biol. and Med.*, 9:77, 1936.

2 Koontz, A. R.: "Congenital Cysts of the Lung," *Bull. Johns Hopkins Hosp.*, 37:340, 1925.

3 Schenck, S. G.: "Congenital Cystic Disease of the Lungs; a Clinico-pathological Study," *Am. J. Roentgenol.*, 35:604, 1936.

4 Miller, W. S.: Quoted by Freedman, Eugene.[9]

5 Maier, H. C.: "Pulmonary Cysts," *Am. J. Surg.*, 54:68, 1941.

6 Naclerio, Emil and Langer, Lazaro: "Pulmonary Cysts; Special Reference to Surgical Treatment of Emphysematous Blebs and Bullae," *Surgery*, 22:516, 1947.

7 Hayashi, J.: Quoted by Freedman, Eugene.[9]

8 Allison, P. R.: "Giant Bullous Cysts of the Lung," *Thorax*, 2:169, 1947.

9 Freedman, Eugene: "Emphysematous Blebs and Bullae," *Am. J. Roentgenol.*, 35:324, 1936.

10 Leach, J. E.: "Pneumothorax in Young Adult Males; Descriptive Statistics in One Hundred and Twenty-six Cases," *Arch. Int. Med.* 76:264, 1945.

11 Kjaergaard, H.: Quoted by Freedman, Eugene.[9]

12 Hering-Breuer: Quoted by Allison, P. R.[8]

13 Head, Jerome: Personal communication to the Author.

Discussion

FRANCIS WOODS, M.D.

Brookline, Massachusetts

Pulmonary cysts of all types present an essentially similar problem. Dr. Clagett's classification of all into bronchial and alveolar cysts is practical. Bronchial cysts are usually single and therefore a simpler problem. Alveolar cysts are usually multiple and therefore a difficult problem for curative therapy. It is only possible if the disease is to some degree localized. Why some individuals develop diffuse dilatation of all or many alveoli, and others of only a few, is not clear. The symptoms in either case are primarily dyspnea and gradual decrease in pulmonary function. Surgical therapy of alveolar cysts is possible when the overdistended alveoli or at least the major group of them are confined to a relatively isolated part of the lung. Excision of the smallest possible number which will give relief of symptoms is the ideal therapy, thus preserving as much normal function of the lung as possible. At times, this may mean pneumonectomy, and at times lobectomy. As often as possible the excision should be confined to a segment or even to the cyst itself, removing no normal lung tissue.

O. E. EGBERT, M.D., F.C.C.P.
El Paso, Texas

It might be worth while to mention the simple treatment resorted to in the case of a young man who had had three accidents of spontaneous pneumothorax over a spread of five years. I managed the last two of these episodes. When the third one occurred I continued to maintain the pneumothorax artificially for a period of three months. I hoped to get sufficient pleural changes from continuing the pneumothorax to insure complete obliteration of the pleural space on re-expansion of the lung, thereby preventing any subsequent pleural accident. To insure sufficient pleural stimulation I introduced on one or two occasions 10 per cent gomenol in mineral oil, each time getting a mild febrile response and a small amount of effusion. After complete re-expansion had occurred x-ray inspection showed definite fogginess of the pleura, suggesting that the desired obliteration of the pleural space had been attained. Ten years have passed since this treatment and no other pleural accidents have occurred. Perhaps the presence of the air alone, from maintaining artificial pneumothorax for the three month period, would have sufficed to produce pleural obliteration, but regardless of the degree of pleural stimulation, it seems rational to deliberately produce obliteration of the pleural sac as treatment for recurrent spontaneous pneumothorax.

RICHARD MEADE, M.D., F.C.C.P.
Grand Rapids, Michigan

I only want to rise to second completely and approve of everything that Dr. Clagett has said. I would like to bring out two other points. He referred to the work of Dr. Head and Dr. Avery. In those cases in which there is pronounced dyspnoea and patients are confined to bed the use of the Monaldi suction drainage will produce remarkable results. In other patients who are not so crippled I would agree that by far the preferable procedure is thoracotomy to determine the exact nature of the lesion. There is one more point I think worth mentioning; that is, in some of these cases in which there is a spontaneous pneumothorax of some standing, that even though you may correct the defect, the fistula may be closed, the lung will not fully re-expand because of an encasing membrane. In such cases it is necessary to do a decortication. If one does that, even though it may leave in the lung multiple cysts which may later rupture and, if there is a free pleural space, cause pneumothorax, after operation the lung re-expands and becomes adherent to the chest wall thereby completely obliterating the pleural space permanently.

Closing Remarks

O. Theron Clagett, M.D.: I would like to thank the discussers of my paper. In regard to the question of putting oil into the pleural space as an irritant and maintaining pneumothorax over a period of some time as a means of treating spontaneous pneumothorax due to blebs and bullae, I do not think it is a very satisfactory treatment. Even without an irritant in the pleural space, some of these lungs that have been collapsed become covered by a fibrous film and decortication is necessary before the lung can be re-expanded, and an irritating oil would certainly result in a lung whose expansion would be prevented by fibrous reaction requiring decortication.

Tetralogy of Fallot: Surgical Treatment

A. RODRIGUEZ DIAZ, M.D., F.C.C.P. and H. ANIDO, M.D.
Havana, Cuba

Since Blalock published his first report on the surgical treatment of pulmonary stenosis, we became greatly interested in this subject.

While performing an necropsy on a ten year old child who had tetralogy we found an abnormal vessel which connected the left subclavian and left pulmonary arteries (Fig. 1); this vessel had a very small lumen and evidently was unable to supply enough oxygenated blood to counteract the cyanosis. Nevertheless, this observation was a vivid proof that Nature, in order to overcome the disabling effects of cyanosis, used the same procedure that Taussig advocated.

Last year we started to operate on cases of tetralogy having dealt, up to now, with 17 cases which are summarized in Table 1. We are aware, of course, that with this meager experience no conclusions whatsoever can be drawn, but we wish to stress some practical points which evolved from our work.

At the outset we had to decide between the two operations which following Taussig's conception were developed to improve the physiologic status of these cyanotic patients: Blalock's and Potts'.

Blalock's technic seemed more advantageous considering the fact that if we had an accident the operation could be interrupted at any stage without any major complication; furthermore, should the follow-up of these patients show the inadequacy of the surgical ductus arteriosus to solve the abnormal physiologic situation or should well known complications of the congenital patent ductus, such as subacute bacterial endocarditis, arise we could proceed to treat these cases as we do with any patent ductus. That much cannot be said of Potts' operation.

To establish a sound comparison, both technics should have been performed in the same number of cases; we have not done so on account of the scarcity of Potts' clamps which were not available until very recently.

Although the teralogy of Fallot is described as a fairly standard syndrome, there are all varieties and variations of the conditions of this condition, all of which are not amenable to surgical treatment. It is obvious therefore that an accurate diagnosis is an essential prerequisite to consider the surgical possibilities of a case of tetralogy.

An accurate diagnosis may only be accomplished by two methods: angiocardiography as described by A. Castellanos and catheterization of the heart as described by Cournand.

We have used angiocardiography routinely and have wondered why it is not widely used in the United States. Its technic is simple and may be easily mastered. It renders valuable information such as the position, size and shape of the heart chambers and great vessels (Fig. 2).

This method avoids many surgical fatalities in cases where practically all the pulmonary flow enters the lung through collaterals of the bronchial artery, which have to be divided in exposing the pulmonary artery for anastomosis. If we divide all these collaterals and there is complete abscence of the pulmonary artery,

TABLE 1

Case	Age in Years	Operation	Position of Aortic Arch	Operative Approach	Dead	Alive
1	8	Blalock	Right	Left	—	+
2	3	Blalock	Right	Left	+	—
3	7	(1)	Right	Left	—	+
4	6	Blalock	Right	Left	—	+
5	9	(2)	Left	Right	—	+
6	6	Blalock	Left	Left	—	+
7	6	Blalock	Right	Left	—	+
8	10	Blalock	Right	Left	+	—
9	4.5	Blalock	Left	Left	—	+
10	3	Blalock	Left	Right	—	+
11	8	Blalock	Right	Left	—	+
12	8.7	Blalock	Left	Right	—	+
13	4	(3)	Left	Right	—	+
14	10	Blalock	Right	Left	—	+
15	11.4	Pott's	Left	Left	—	+
16		(4)			—	+
17	4	Blalock	Left	Left	—	+

(1) Ligation and section of persistent left cava superior.

(2) No pulmonary artery found.

(3) When the pleura was opened, the patient developed an auricular fibrillation; blood pressure fell to zero. Cardiac massage was performed. Intravenous digitalis was given. Recovery ensued after half an hour. The operation was postponed.

(4) Same case as referred in No. 13; developed same complication while receiving anesthesia.

acute anoxemia develops and death ensues. Blalock refers 18 fatalities following operations in which it had been impossible to find a pulmonary artery and Humphreys one. If these patients had had a preoperative angiocardiography it would have shown the abscence of the pulmonary artery and the operation would not have been performed.

The location of the aorta may be exactly determined by angiocardiography and in some cases we have been able to measure the length of the subclavian artery.

This procedure may be performed at any age, has no complications and the only warning we have to report from the surgical point of view, is to defer the operation at least a week after its performance, because it increases bronchial secretion.

Catheterization of the heart is a cumbersome affair that cannot be used as a routine examination. It necessitates a special team to produce satisfactory results although we must recognize that in the hands of such a team it yields invaluable information. It entails some risk and fatalities have been reported. It requires the joint work of a cardiologist, anesthetist, cardio-vascular surgeon, physiologist, chemist and radiologist and, at least at present, should be reserved for research centers.

We have not used any particular preoperative preparation. The anesthesia has been intratracheal with cyclopropane and oxygen. If we have extrasystoles we change to ether. To facilitate the intratracheal intubation we have not hesitated to use 1 or 2 cc. of curare intravenously, without any untoward effects.

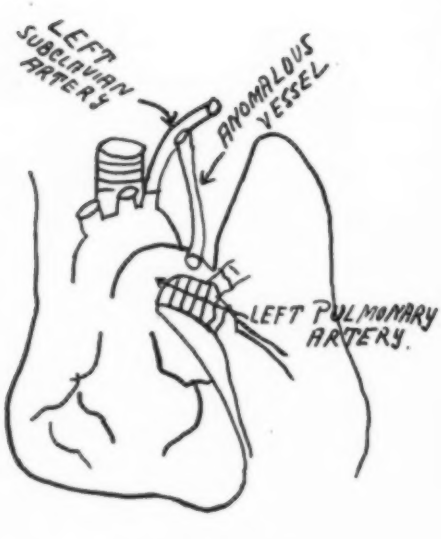


FIGURE 1

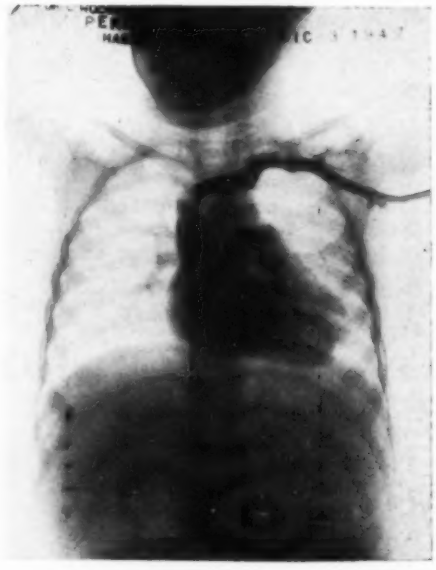


FIGURE 2

An approach through the third intercostal space, similar to that of anterior thoracotomy is used. Lately we have tried the posterolateral approach through the fourth intercostal space and find it highly satisfactory, because the dissection of both arteries, pulmonary and subclavian, is easier and the anastomosis may be performed smoothly as we have a clean access to the anterior and posterior aspects of the suture.

Blalock recommends that the incision should be made on the side opposite that on which the aorta descends. We have broken this rule in cases where the angiocardiography showed a short right subclavian. We recognize that the subclavian artery branch of the innominate provides a better angle for the anastomosis than the subclavian branch of the aortic arch, but the latter can function satisfactorily supplying enough blood to improve the cyanosis.

The exposition of the left pulmonary artery is simpler than the right. It is the highest structure of the pedicle; it runs a straight course towards the lung and can be distinctly isolated from the veins; it is the only vessel that surrounds the superior lobe on its way to the interlobar fissure. Such is not the case with the right pulmonary artery which springs up from the pedicle following an upward course and divides in two branches almost at the outset.

The vena cava should be continuously retracted in this dissection and sometimes the pulmonary veins too are in front of the artery and extreme caution must be exerted not to confuse them, as has been the case in Blalock's experience.

All these considerations led us to the thought of advocating the left side approach systematically. If we find a good subclavian which may be anastomosed to the pulmonary artery with a good angulation we perform the Blalock operation, if we do not we turn to Potts' technic. This procedure, which we followed in the last case operated on, enables us to avoid having to perform the anastomosis using the carotid artery, with its high percentage of cerebral complications.

The vagus nerve is routinely injected with 2 cc. of 1 per cent novocain to avoid reflexes. In order to procure an adequate length of the subclavian artery we repeatedly have ligated the inferior thyroid, vertebral and even the internal mamary arteries, with no embolic or thrombotic complication.

The incision on the pulmonary artery is done transversely whenever it is possible; if not, we resort to the longitudinal incision.

We have not used more than 250 cc. of plasma during the opera-

tion; no other infusion has been administered, from our second case on.

The postoperative course has been uneventful. The two deaths reported in Table 1 correspond, one to a vago-vagal reflex during the dissection of the subclavian artery; it appears that the nerve had not been properly injected; the second fatality occurred four hours after the operation. The necropsy revealed nothing but a marked pulmonary engorgement. We feel that this baby died due to an overdose of saline solution.

Case 3 had a persistent patent left vena cava superior, which opened in the left auricle, with a coexisting tetralogy of Fallot; this anomaly was distinctly shown by the preoperative angiocardiography (Fig. 3). This boy had our highest hematocrit reading: 91 per cent. The performance of Blalock's operation was considered but finally we decided that the division and ligation of the left vena cava superior would reduce the amount of blood with a low level of oxygen saturation returning to the heart, with a subsequent amelioration of cyanosis.

Following the operation (Fig. 4) the hematocrit reading dropped to 56, the cyanosis diminished and the well being of the patient was notably improved.

We have seen this patient two months after the operation and the contrast with his preoperative status is remarkable, especially relating to his working capacity. This boy, who hardly could walk without a fainting spell, is now able to play base ball.

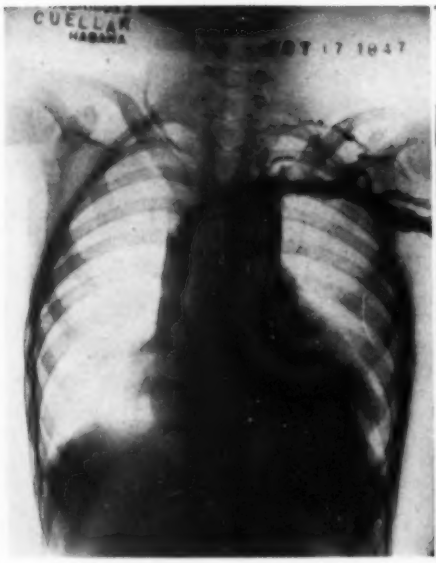


FIGURE 3

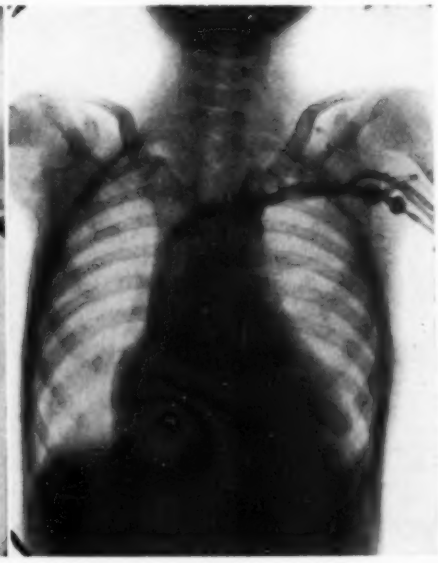


FIGURE 4

SUMMARY

Seventeen patients with tetralogy have been operated on with a mortality rate of 11.6 per cent.

The value of angiocardiography is emphasized, and its use is recognized as a routine exploration. It avoids fatalities in cases where no pulmonary artery is found.

The operation of a case of persistent left vena cava superior, opening in the left auricle, is reported.

The left thoracic approach and postero-lateral incision are recommended as they give the alternative of performing either Blalock's or Potts' operation.

SUMARIO

Se presentan diecisiete casos de Tetralogía de Fallot, operados con una mortalidad de 11.6 por ciento.

Se hace especial hincapie en el valor de la angiocardiografía, la cual se preconiza como una exploración de rutina. Su empleo evita la muerte de aquellos casos en que disecado el pedículo pulmonar, no se encuentra arteria pulmonar.

Se reportó la operación de un caso con vena cava superior izquierda, la cual desembocaba en aurícula izquierda.

Se recomienda el acceso por hemitórax izquierdo, así como la incisión posterolateral, ya que de este modo si no se puede practicar la operación de Blalock, se hace la de Potts.

Addendum: Since this paper was written, 11 additional patients have been operated on with one fatality, which yields a mortality percentage, considering the whole group, of 10.7 per cent.

REFERENCES

1 Taussig, H. B. and Blalock, A.: "The Surgical Treatment of Malformations of the Heart in which there is Pulmonary Stenosis or Pulmonary Atresia," *J.A.M.A.*, 128:189, 1945.

2 Cournand and Col.: "Measurement of Cardiac Output in Man using Technique of Catheterization of Right Auricle or Ventricle," *J. Clin. Invest.*, 24:106, 1945.

3 Potts, W. J., Smith, S. and Gibson, S.: "Anastomosis of Aorta to Pulmonary Artery; Certain Types in Congenital Heart Disease," *J.A.M.A.*, 132:627, 1946.

4 Humphreys II, G. H.: "The Diagnosis and Treatment of Congenital Cyanotic Heart Disease," *Bull. New York Acad. Med.*, (May) 1947.

5 Clagett, O. T.: "Surgical Considerations in Tetralogy of Fallot," *Proc. Staff Meet., Mayo Clinic*, 22: No. 9, 1947.

6 Murray, G.: "Surgical Treatment of Congenital Heart Disease," *Canad. M. A. J.*, 58:10, 1948.

7 Castellanos A., Pereiras R. y García, A.: "La Angiocardiografía," *Archivos de la Soc. de Estudios Clínicos de la Habana.* Tomo XXXI, Núms. 9-10, 1937.

The Importance of Various Mechanical and Circulatory Postoperative Pulmonary Complications

LOUIS F. KNOEPP, M.D., F.A.C.S., F.C.C.P.*
Shreveport, Louisiana

Pulmonary diseases constitute some of the most feared complications in the practice of the general and thoracic surgeon. They have been stated to occur in 2 to 4 per cent of all surgical patients and in 10 per cent of all abdominal operations. Moreover, of all surgical patients it is said that 0.6 per cent will die of some pulmonary malady. Since the advent of the chemotherapeutic and antibacterial drugs, the incidence would seem to be less, but their occurrence is still of sufficient gravity to warrant discussion.

The majority of pulmonary hazards can be conveniently classified under three headings: mechanical, infectious, and circulatory. All such disorders begin as any one of the three, but due to the intimate relationship of the pulmonary broncho-vascular structure and lymphatic lung network, a complexity of affliction may result. For instance, pulmonary infarction may easily be found the forerunner of pneumonia, abscess may lead to atelectasis, also, atelectasis may be seen to accompany either the infectious or circulatory diseases.

Although the most prevalent postoperative pulmonary complication would seem to be bronchopneumonia, we are less concerned with its appearance than we are with the more basic phenomena which predispose to it. A goodly number of these cases can be ascribed to invasion of a virulent organism in a host of lowered resistance. Naturally, many infectious processes seen postoperatively have their origin in an unrecognized inflammatory disease that was present preoperatively. This may be evidenced by simple nasopharyngitis, sinusitis, or bronchitis. Other chronic pulmonary infections as bronchiectasis and lung abscess have been ascribed as causative factors of seemingly acute postoperative complications.

We should like to recall three theories which have been proposed in the past to explain the onset of pneumonitis postoperatively: namely, (1) Whipple's theory of aspiration pneumonia, (2) the theory of infected emboli proposed by Lichtenburg, Cutler, and others, and (3) Corylios' contribution on atelectasis. Although the first two were well founded, an overwhelming amount of material

*From the Veterans Administration Hospital, Alexandria, Louisiana.

has favored Coryllos' theory. He showed that there were pneumococci present in 72 per cent of the tracheae of all operated patients but that these organisms were present 100 per cent of the time in those patients who developed atelectasis. The secretions harboring pneumococci were found to be more viscid and therefore more difficult to eliminate than ordinary bronchial secretion. The further work of Cooper and his associates in differentiation of these pneumococci showed every conceivable type present.

Atelectasis

The most important clinical entity as a mechanical factor is atelectasis. Its seriousness is convincingly shown in the report of Christopher and Shaffer who found upper respiratory disease prevalent in 30 per cent more patients with it than without it.

What are the causes of atelectasis? Experimentally, it has been produced in a number of ways. After the work of Faulkner and Faulkner on mucus plugs, Lee, Tucker and Clerf reproduced it in dogs by inserting such plugs into one stem bronchus with the aid of a bronchoscope. The most significant finding was an absorption of air beyond the point of obstruction producing collapse of the alveoli. Galbraith and Steinberg, on the other hand, produced atelectasis without first producing bronchial obstruction. Approaching it from an entirely different angle, Scott and Ivy postulated a nervous reflex which causes venous engorgment in the lung, coincidental with a bronchiolar spasm. In still another contribution, histamine was stressed as a factor in the production of atelectasis. This substance, although present in large amounts in normal lung tissue was not found by Lindskog to be eliminated by fixation and storage in the lung but "probably by the hydrolytic action of histaminase in blood and tissues." Although histamine can produce bronchiolar constriction, it would seem to account for very few, if any, of the usual run of cases seen postoperatively. While the importance of pulmonary stasis and nervous reflexes is granted, we believe the greatest importance lies in the mechanical plugging of the bronchi with mucus, since elimination of this factor with the bronchoscope usually results in prompt aeration of the affected segments of the lung.

This brings us to a consideration of some of the causes of atelectasis in surgical patients.

1) Bronchial occlusion: We refer to the presence of known or unrecognized intrabronchial and extrabronchial diseases which may materially narrow the lumen of the bronchus. This may constitute mucus plugs, tumors, foreign bodies, stenosis, granulations, enlarged lymph nodes, effusions, aneurysms, abscesses, or virtually any inflammatory process producing sufficient edema

to compress or reduce the caliber of the bronchus. The most frequent of these in postoperative patients is the mucus plug. Blood in the bronchi was found to be a pertinent cause of atelectasis in 79 per cent of the tonsillectomies analyzed by Myerson. Asthma with its bronchial narrowing was found to be a background in 10 per cent of all postoperative atelectasis.

2) Inability of the patient to cough: After anesthesia has been administered, patients who do not raise accumulated secretions from the bronchi may be unable to do so for many reasons. (a) Coma: This might concern excessive preoperative medication, cerebral accidents, diabetic coma, or the depth and duration of the anesthetic itself. In a remarkable study of 7874 operations at the Wisconsin General Hospital, Rovestine and Taylor found that those lasting 1 hour or less had from 50 to 100 per cent fewer pulmonary complications than those lasting from 1 to 1½ hours. As the duration of the anesthesia increased, the morbidity also increased to the point wherein those lasting 2 hours had three times the number of complications while those lasting over 3 hours showed 31 per cent with some pulmonary complication. (b) Type of anesthesia: It is not necessary to have a loss of consciousness in anesthesia to reduce the cough mechanism. Many reports cite a higher incidence of atelectasis from spinal anesthesia than from general anesthesia. One of the factors thus responsible is the paralysis of the lower intercostal muscles that this agent produces. Inhalation agents on the other hand produce certain irritating effects on the bronchi when used over a long period of time which are not present with the injection agents. (c) Severe postoperative pain: Patients who suffer intense abdominal or thoracic pain are not willing to cough. Upper abdominal incisions are more painful than lower abdominal incisions. In King's study, laparotomies and hernias produced 14.3 per cent pulmonary complications as compared to 1.2 per cent in all other surgery. In this connection, wounds that heal per primum produce fewer lung complications. King thus found that clean appendectomies were followed by pulmonary complications in only 7.1 per cent, while infected cases with drainage had a pulmonary morbidity of 27.9 per cent. (d) Position during surgery: This concerns the degree of inclination of the thorax during and after the operation. If secretions are present, the head-down position is more apt to keep bronchial secretions drained than any other position. Gray noted that he could reduce postoperative atelectasis by as much as 30 per cent when the Trendelenburg attitude was maintained during the operation and for the next 24 hours thereafter. (e) Miscellaneous causes: Ineffective cough may be the result of insufficient strength. Patients who are por surgical risks fre-

quently lack the vitality for an adequate cough reflex. This conforms to Henderson's belief that hypoventilation of the areas of the lung was due to a general reduction in muscle tone and subsequent diminution in tidal volume. Tight abdominal binders have been known to hinder the cough mechanism particularly in the lower lung fields. Paradoxical respiration as seen in thoracic injuries and operations may disturb the stability of the thorax so that cough is ineffectual. The administration of heavy doses of atropine and/or maintaining the patient in negative fluid balance may thicken bronchial secretions sufficiently to prevent their expulsion. Patients who are chronic smokers are apt to have tenaceous mucus. Included in this category are those cases of bronchiectasis who are unable to empty their bronchi completely of mucopus.

3) Location of the incision: Upper abdominal incisions favor limitation of the lower half of the thorax and may contribute in this way to a higher percentage of atelectasis. Pasteur laid emphasis on the rise of the diaphragm, and more recently Overholt and Veal have recalled its importance. In this connection, the diaphragm was found to be elevated in 93 per cent of patients undergoing abdominal surgery. Significantly enough, Churchill and McNeil noted that its elevation reduced vital capacity some 30 to 50 per cent.

4) Operative trauma: An abdominal reflex was described by Goltz and again by Scott and Ivy which results in a viscerocardiac inhibition. When these investigators tapped on the abdominal organs of animals or pulled on the viscera, there was a definite stasis of general and pulmonary circulation and a coexistent bradycardia. This was often accompanied by temporary apnea. These latter two factors were all that Galbraith and Steinberg had found necessary to produce atelectasis experimentally.

What are the clinical features of atelectasis and how can it be recognized? When our attention is called to such a patient, it may be for either an elevated temperature, tachycardia, dyspnea or cyanosis. A combination of these symptoms and findings may frequently exist. These patients are listless and are unwilling to move, even in the bed. If they are conscious, as most of them are, they act as though they were afraid to move. They frequently have pain particularly at the operative site. Some have chest pain. This pain plays a dominant role in their immobility and feeble effort to cough. If they do cough, it is weak and ineffectual. In our experience, patients who cough effectively and unhesitantly rarely develop atelectasis.

Physical signs are present some time before roentgen findings are demonstrable. Cyanosis and dyspnea are prominent and there

is a noticeable limitation of motion of the portion of the chest affected. Temperature and pulse are usually elevated conspicuously over expected postoperative levels. The percussion note may be dull if the process is localized. The early stages in the dry form may show only diminished breath sounds, but after secretions have been dammed back for some time, rhonchi may be audible without the aid of the stethoscope. The retained mucus may be heard as high as the stem bronchus or trachea and may be found more easily by rotating the patient on the uninvolved side. Mediastinal shift to the side of collapse may often be demonstrated by palpating the cardiac apex impulse. Occasionally, the act of turning the patient in this way will promote drainage and ventilation to the hypofunctioning lung and literally clear the process while one is attempting to make the diagnosis.

Little need be said about the roentgen diagnosis of atelectasis. Films may present findings of either a patchy or massive process. The former finding may be fairly diffuse after the condition has existed for a time when secretions have been forced into other parts of the lung. Not infrequently the demarcation between atelectasis and a pneumonic process is ill-defined. Attention is called to the oft-missed retrocardiac type which may require special views for demonstration.

If the preceding observations are significant, then a certain regimen can be set forth which will materially lower the probability of occurrence of atelectasis. If such a complication does occur, it can best be managed during its formative stage.

Preoperative roentgenograms should always be taken. Pulmonary disease is better diagnosed by the use of the x-ray before complications have developed. In most institutions these films are routine practice and frequently denote pulmonary disease when the clinician is unable to detect it by physical signs. It is also advisable to complete whatever diagnostic studies are indicated by unexplained roentgen shadows. We refer particularly to the use of bronchograms and the bronchoscope for the clarification of suspected intrabronchial changes.

In the preoperative preparation of the patient we are chiefly concerned in sending him to surgery with as normal a respiratory apparatus as possible. Naturally, operation in any patient with evidences of upper respiratory infection is postponed until such a process clears. Unless uncontrollable, it is likewise best to postpone operation in patients who have hemoptysis until this symptom abates. In bronchiectatic patients, as well as chronic smokers, postural drainage is emphasized to clear the bronchi of all secretions possible. Ammonium chloride a day or two before surgery often enhances the elimination of viscid secretions by

promoting liquefaction. Some patients are given prophylactic antibiotic or chemotherapeutic medication for 24 to 48 hours before operation. Although statistics are not readily available, we believe the use of these drugs has "paid off" in preventing a certain proportion of pulmonary complications.

In the operating room we concern ourselves chiefly with the depth of narcosis. Excessive preoperative medication is condemned and atropine is never ordered unless for definitive reasons. The anesthesia is selected to meet the needs of the surgeon without increasing the operative risk. Some operators, in order to obviate prolonged anesthesia, delay induction until the operative site has been prepared and the field sheets placed. The patient may be placed in Trendelenburg's position to facilitate drainage of bronchial secretions. When the lateral recumbent position is necessary, as in renal or thoracic surgery, the head-down position can be attained just as easily as when the patient is in the dorsal position. The only contraindication to Trendelenburg's position would appear to be in cases of abdominal suppurative processes where dependent drainage toward the iliac fossa is desired. However, this may be a point for conjecture. During the operation the care of the tracheobronchial tree is in the hands of the anesthetist. Needless to say, a well-trained individual will make every effort to keep secretions free by frequent use of the aspirator, with or without an endotracheal tube. The avoidance of excess secretions can be frequently managed by careful selection and use of various inhalation agents. It would appear to us that expert anesthesiologists have less difficulty with excessive secretion formation than a less qualified technician.

After operation, tight adhesive strapping is avoided and the lower thorax is never incorporated tightly in the dressings. The anesthetist should routinely arouse the patient by the use of 10 per cent carbon dioxide in oxygen. This promotes hyperventilation of all segments of the lung and tends to loosen mucus plugs from the bronchial apparatus. It is also beneficial in arousing patients to a state of consciousness where they can cough forcibly. We always demand that the patient cough before leaving the operating theater. Trendelenburg's position is maintained until the patient reacts sufficiently. After this time, frequent change of position is recommended even to a semi-Fowler's position where some patients expectorate more effectively. Patients who cannot be aroused promptly, e.g. under ether narcosis, may be subjected to bronchoscopy. This is particularly true after thoracic operations.

Postoperatively, patients are encouraged to cough periodically every 3 hours for the first few days. If they are unable to do so, we again resort to carbon dioxide inhalations. If mucus still per-

sists, we next resort to a change of position; older writers spoke of this in the prevention of "hypostatic pneumonia." By turning the patient alternately on the uninvolved side for 30 minutes then 15 minutes on the involved side, we can help to promote drainage from the uppermost lung and obviate pulmonary venous stasis. Not infrequently, patients are aided to a sitting position to effect this change. If this is not entirely effective or if signs of atelectasis become evident, we next suggest the use of intratracheal suction as described by Haight. This is a valuable maneuvre that should be known by every postoperative team. It is repeated every 4 to 6 hours until the cough reflex becomes well established. Very frequently, tracheal aspiration can be begun in the operating room if an endotracheal tube is in place. The anesthetist merely inserts a small rubber catheter attached to the suction machine. There are times however when one must resort to bronchoscopy to remove mucus out of reach of the catheter and we do not hesitate to have a unit at the bedside in readiness when the patient develops signs of impending atelectasis. We feel that its use has aborted an otherwise certain bronchopneumonia in many instances. The use of steam inhalations is of definite value in thinning secretions sufficiently that the patient can expel them. Ephedrine at times is also helpful in enlarging the bronchial lumen when a certain degree of spasm or edema exists. We also recommend the use of multiple intercostal block as advocated by Bartlett and others for the control of thoracic pain and thereby facilitate cough.

Most thoracic patients are routinely placed on penicillin therapy postoperatively. In the event of atelectasis the dosage of this agent is increased to conform to therapeutic standards. Then again, one may employ streptomycin or one of the chemotherapeutic drugs depending on the type of organism found in the sputum. It has been definitely shown that the effective time to use these drugs is early in the disease and we employ them to the fullest extent in threatened pneumonic cases.

The following case illustrates some of the points previously outlined, even though the patient was handled long before we were fully aware of all the factors responsible for postoperative pulmonary disease.

Mrs. F.B., a white female, age 31, was already under hospital care for tuberculous peritonitis with ascites. She had been in the hospital some 27 days when on May 4, 1936 she suddenly developed signs of intestinal obstruction. After meager preoperative preparation including 1000 cc. of intravenous fluid, she was subjected to exploratory laparotomy under spinal procaine (150 mg.) anesthesia. The operation was carried out in the head-down position and no supplementary anesthesia was used. The operator found diffuse inflammation of the entire peritoneum with

thickened plastic exudate surrounding the adnexae and small intestine. This was most pronounced in the area of the cecum and ascending colon where the adhesive process appeared to be producing more obstruction than at other portions of the bowel. A cecostomy was performed and a few adhesions liberated, but it did not appear that this would be too successful in freeing much of the obstruction. The outlook was considered hopeless and the abdomen closed in routine fashion. Her postoperative course was complicated by a temperature rise to 103 degrees F. within 24 hours. The respiratory rate was 30 and the radial pulse 130. One could hear only distant breath sounds in the lower portions of both lungs accompanied by frequent harsh rales. She refused to cough effectively. Ten per cent carbon dioxide in oxygen was administered without apparent benefit. Unhesitantly, she was subjected to bronchoscopy and large amounts of thick tenaceous mucopurulent secretion removed from both lower lobe bronchi. A roentgenogram of the chest then showed a patchy atelectasis in both lung bases but the lung was fairly well aerated. Following bronchoscopy, breath sounds were heard equally well in all portions of the chest with only an occasional rale, and within 24 hours the temperature was 99.4 degrees F. and the respiratory rate 22. Thereafter, she was able to cough effectively, and this was encouraged at repeated intervals of 4 hours until the 5th postoperative day. At this time she was afebrile and aside from a slow convalescence from complete obstruction and supplemental parenteral fluids for some 19 days she made an excellent recovery. Check-up roentgenogram of the chest after 21 days showed normal clearing in all portions of the lung. She remained in the hospital 92 days after operation, still convalescent from tuberculous peritonitis.

We feel that aside from the grave situation in the abdomen of this patient, her complication of atelectasis would have surely resulted in bronchopneumonia from which she could not have recovered. We credited a prompt bronchoscopy to correction of this otherwise unavoidably fatal complication.

An additional case is presented to illustrate further the prophylactic care instituted against atelectasis, and the shortcomings of such a preventitive regimen in the occasional case.

Mrs. R.B., a white female, age 21, had a 6 months' history of cough and loss of 8 pounds in weight. There was no hemoptysis. The family history revealed no tuberculous contacts or deaths. Her past history portrayed a pneumonia in infancy and no other serious illness. Her menstrual history was normal. Examination revealed a thin young adult female who was 62 inches tall and weighed 89 pounds. The radial pulse was 90 and the blood pressure 136/90 in the right arm. Physical findings were abnormal only in the examination of the chest. Occasional rales were heard anteriorly and posteriorly over the right apex. Laboratory findings were significant only in the finding of acid-fast bacilli in the sputum. The roentgenogram of the chest taken on the day of admission (November 15, 1946) showed a 4½ centimeter cavity in the right upper lung extending down to the 5th interspace posteriorly. Except for a small surrounding zone of inflammation, other portions of the lungs were within normal limits.

A trial of pneumothorax was ineffective. She was subjected to bron-

choscopy in anticipation of thoracoplasty, to rule out tracheobronchial tuberculosis. The findings were normal. On January 11, 1947, under cyclopropane-oxygen anesthesia and in slight Trendelenburg position, a 2½ rib right thoracoplasty was performed. The operation proceeded in a normal fashion and without significant departure in the blood pressure or respiratory graphs. After the patient was turned to the dorsal position, she showed signs of moderate cyanosis and one could hear rhonchi in the region of the trachea. Inasmuch as an endotracheal tube was not in place, she was bronchoscoped at once, and a moderate amount of mucopus removed from the trachea and both stem bronchi. Breath sounds then appeared fairly normal and she appeared to be ventilating the left lung adequately. The first 18 hours postoperatively were uneventful but she then began again to show cyanosis, dyspnea, an elevated pulse to 130 and a temperature of 102.2 degrees F. orally. Auscultation revealed distant breath sounds over the entire left lung. Cough was feeble and unproductive. A roentgenogram revealed complete atelectasis of the left lung with moderate shift of the trachea to the left. The only ventilating portion of the lung was in the lower right chest. Oxygen was administered by BLB mask to relieve cyanosis and she was subjected to intratracheal suction. This was effective in raising a few thick plugs of mucus after which one could hear breath sounds much clearer in the left lung. She was unable to breathe in any but semi-Fowler's position and the routine of change of position was abandoned. Temperature continued to rise to 105 degrees F. but the pulse remained at 130. She seemed to be breathing comfortably and continued to cough effectively. Sputum culture at this time revealed many pneumococci and the postoperative dose of penicillin was increased to 40,000 units every 3 hours. By the 4th postoperative day, the temperature suddenly fell to normal and the oxygen was discontinued. Penicillin was continued for 3 more days. A check-up roentgenogram on the 7th day revealed nearly complete clearing of the entire left lung and she was transferred to her sanatorium on the 10th postoperative day. She went through her succeeding two stages of thoracoplasty without event and eventually was discharged from the sanatorium with sputum cultures negative for acid-fast bacilli. The roentgenogram showed evidence of cavity closure and the left lung remained clear of any pathology.

This is a case of diffuse lobar pneumonia which was initiated by atelectasis of the left lung. This complication developed in spite of the bronchoscopic intervention to avoid it, but we believe that the patient withstood her pneumonia with a brighter outlook than if we had not enforced such detail in her postoperative care. One might theorize that she was developing an upper respiratory infection at the time of surgery but we believe that bronchial obstruction from the mucopus was a more likely cause.

Spontaneous Pneumothorax

Of not occasional interest is the occurrence of pneumothorax in operative and postoperative cases. The causes of pneumothorax may at times be quite certain as in various forms of pulmonary disease, but at other times one may be quite at a loss to find any

definite etiologic reason. Of the many thoracic conditions which may produce this complication, tuberculosis leads. Certain cancerous lesions of the pleural surface of the lung, cystic disease, or any inflammatory process near the pleura may harbor the underlying lesion. The mechanism of the aforementioned diseases is usually by tear of an adhesion which also tears the lung, allowing air to enter the pleural cavity. Blebs on the surface of the lung have been known to rupture spontaneously without adhesion formation. Reports have reached the literature wherein excessive positive pressure with anesthetic machines caused rupture of the lung, trachea or bronchi with resultant pneumothorax. Phillips reported one such case occurring bilaterally. Stephens noted 3 cases of pneumothorax in thoracic operations occurring on the contralateral side. The mechanism here was undoubtedly one of tearing the mediastinal pleura during dissection. Any operation in which an attack is made on the pleura, either purposefully or inadvertently, may result in pneumothorax. Special mention is made of nephrectomy and lumbar sympathectomy where the lower border of the pleura may not be clearly seen. This complication has even been reported following bronchoscopy.

The onset is usually quite sudden and dramatic. If the patient is awake, there is usually a severe stabbing pain on the affected side of the thorax. This is followed shortly by dyspnea of a varying degree. If a valvular action results from the tear in the lung, the air may continue to fill the thorax and compress the lung. A splinting action of the abdominal muscles may accompany such a process, and acute intra-abdominal disorders have often been mistakedly diagnosed. Rolleston almost subjected a patient to laparotomy for ruptured peptic ulcer with this condition. Dyspnea may be more marked when the patient lies on the uninvolved side, but most patients prefer to remain in a sitting position.

The diagnosis is quite obvious if one's attention is focused on the thorax. Respiratory motion on the involved side is usually greatly decreased and may even be paradoxical. On percussion, the note is tympanitic and auscultation reveals absent breath sounds. The cardiac impulse will be shifted to the side opposite the pneumothorax, and in some cases of left-sided involvement, the heart may lie entirely within the right thorax. The unaffected lung is frequently crowded within its own side of the thorax and one may even see abdominal distention from the displacement of the diaphragm downward.

If dyspnea is marked, one should not wait to confirm findings with the roentgenogram as the process may end fatally in a short time. Without taking time for anesthesia, one should thrust a moderate-gauged needle (17-19) of at least 2 inch length through

one of the accessible interspaces of the involved side even though a syringe or manometer is not available. Where the latter is accessible, one can measure with some degree of accuracy the amount of air withdrawn, together with the pressure within the thorax. Such pressures will read anywhere from neutral to highly positive until pressure is relieved. If a manometer is not at hand, air should be allowed to rush out the needle until the cardiac apex impulse returns to its normal position. Using the pulse as a guide, one can slow the shift of the mediastinum so that circulatory embarrassment does not follow. Too rapid a shift of mediastinal contents will lead to greater tachycardia and eventual cardiovascular collapse. The patient, if awake, feels relieved from the moment the needle enters the thorax. One can then remove the needle and check the position of thoracic organs with a roentgenogram. Repeated withdrawals may be necessary where the fistula is still present. If pneumothorax recurs within a few hours, one may feel safer to leave a blunt-ended needle indwelling within the pleural cavity, connecting the hub of the needle to rubber tubing whose free end is placed under a water trap. An occasional case will require open thoracotomy to close the fistula, but as a rule, most will reexpand fully after a limited number of days or weeks. Stubborn pneumothoraces which do not reexpand readily will frequently form a moderate effusion. This should likewise be aspirated and the pleura kept fairly dry.

The following illustrative case is a fairly common one in the practice of the thoracic surgeon, although most do not end fatally as this one did.

A white male, age 21, was under treatment for a simultaneous left empyema and abscess of the right middle lobe. The previous history was one of upper respiratory infection which did not respond to treatment but resulted in empyema within a few days. This was drained surgically and his condition improved, only to relapse after 7 weeks. Bronchoscopy and transfusions seemed to improve him clinically, but the abscess grew steadily larger and surgical drainage was decided upon. Under local anesthesia the parietal pleura overlying the abscess was exposed with resection of short segments of two ribs. The pleura was packed with gauze due to inefficient symphysis and the wound left open. Suddenly, after 2 hours, he developed marked dyspnea and unconsciousness from which he never recovered, dying within 3 hours. Continuous withdrawal of air from the right pneumothorax and an oxygen tent failed to save him. We attributed death to cardiovascular collapse due to his prolonged illness and augmented by the mediastinal shift. Postmortem exposure of the operative site revealed a spontaneous tear in the pleura, but no projecting rib stump to account for it.

Pulmonary Embolism

In postoperative complications, circulatory phenomena play a much different role. Most of them occur in the form of emboli

or infarcts under most puzzling circumstances. Heretofore, we have regarded these complications occurring in seemingly normal patients. The postoperative convalescence for the first few days had been uneventful and without incident. Suddenly without apparent warning, patients developed marked dyspnea, pallor or cyanosis, and signs of profound shock. Death came in a matter of a few minutes to a few hours. Occasionally one would survive but not without a stormy course. Every surgeon has probably witnessed this catastrophe and has been at a loss to explain it to the relatives, let alone to himself. Our supposition that these patients were progressing normally, was, of course, erroneous.

In the first place, these people appear to be constitutionally different than others; they are phlegmatic, may be obese, can be young adults but are more often in advanced age groups, and may run a relatively slow pulse. The latter finding is not too constant, however. Rehn would stress that they are the cachectic type who are chronically ill and are in the upper age brackets. We recognize that patients in the middle or old-age bracket are more prone to develop embolism, but when a young adult becomes the victim, we are impressed no end. Secondly, some of these people have various unrecognized pathological processes which are precursors to embolism. There may be cardiac vegetation, saccular aneurysms or arteriovenous shunts of varying size, or some element of cardiac peripheral decompensation producing venous stasis. They may have seemingly inocuous lesions where thrombi arise, as varicosities of the lower extremity, broad ligament, or prostatic plexus. Evidence of phlebitis may or may not be present or have ever occurred. Rehn refers to the presence of infection, deficiency of liver glycogen, decreased alkali reserve, and circulatory liability as evidenced by control tests. An imbalance of the sympathetic nervous system or possible hormonal imbalance would seem to be one of the responsible factors. Although females are more susceptible than males (3:2), males are more frequent victims of fatal emboli. Barker and his associates found that the occurrence of embolism in blood disorders was 9.3 per cent while those with no predisposing element was only 1.9 per cent. Other diseases in a similar tabulation were significant; embolism occurred in cardiacs in 7.2 per cent, peripheral vein disorders in 5.6 per cent, cancer patients in 4.7 per cent, and severe infections in 5.8 per cent. It is also significant that the rate in obesity was higher; patients weighing over 200 pounds had a susceptibility of 7.1 per cent, while those under 200 pounds developed it in 3.2 per cent.

The third and most significant feature of these cases is that many of them show none of the previous tendencies, and throm-

bosis occurs in apparently healthy subjects. The chief offender in such an individual is venous stasis, brought about by post-operative immobility. One cannot say that the magnitude of operation with impending shock or collapse had anything to do with its predisposition. One is impressed when such a patient succumbs of embolism after a relatively non-shocking and less major appendectomy or hernia repair. The site of the thrombus in such individuals is usually found in the deep popliteal or femoral veins. Homans has shown that autopsies revealed thrombosis in these deep calf veins in over 50 per cent of the cases. These individuals are unwilling to move about during their first days of convalescence. Immobility seems manifest particularly in the lower extremities. About the 7th day or so, when they do arise and move, a weakly organized thrombus is freed, or its projecting free end breaks into the circulation. The circulating thrombus is thus destined to lodge in the pulmonary vascular system. Occasionally, one finds that the thrombus arises from the region of the operative wound, but this is not the rule. Where normal healing involves organization of thrombi in ligated vessels, these individuals for some reason produce propogating thrombi which break easily. If the embolism is small, and vagal impulses are not too severe, infarction of a segment of lung results, with possible eventual recovery. Some patients are subjected to repeated showers of such emboli, and when they appear to have recovered from one episode, another possibly more severe strikes them. If the embolus is large or extensive, it may block a large portion of the pulmonary circulation and a rapid exitus results. There is no significant alteration in the coagulability of the blood in these patients despite reports to the contrary. Although some investigators have found significant alteration in the prothrombin levels of the blood, many show no such abnormality. There is merely a venous stasis, and if there is any other pathognomonic finding in the blood, it does not show by current diagnostic methods.

The basis of sudden death in these cases has been brought out by the experimental work of deTakats and his associates who reproduced embolism in dogs with injections of starch emulsion. Depending on the amount and consistency of the emulsion, two types of embolism were apparent, both comparable to clinical types: (1) massive embolism resulting in death, and (2) precapillary embolism from which the dog might recover if large amounts of emulsion were not used. Typical electrocardiographic tracings resulted from both types in many of the animals, and if the embolus was not too extensive, the dogs could frequently be saved by the use of oxygen and the vagus-blocking drugs (atropine).

The effectiveness of the latter derivatives lay in the former experimental findings of increased pulmonary artery pressure and isolation of receptor fibres by Takino and Watanabe in the adventitia of this vessel. Hypertonus of the vessel elicited excessive stimuli to these fibres which gave typical vagal responses. The terminal effects were cardiac standstill and ventricular fibrillation with a shift of the pacemaker to the A-V node. Such findings are similar to those obtained by coronary occlusion, in fact, there was evidence of decreased blood flow in the right coronary in many of the animals.

An alert surgeon will diagnose this condition long before embolism occurs. Subjectively, complaints are minimal but present. There is vague leg pain accompanied by tenderness in the outer posterior aspect of the calf. Objectively, there is pain in the calf on dorsiflexion of the foot (Homans test) and there may be local tenderness over the femoral triangle. Likewise, mild cyanosis and edema of the foot may be manifest when the member is in the hanging position. Such a calf is usually firmer and feels more unrelaxed than the corresponding normal leg. The calf should be measured frequently to denote changes in inequality. Pulse rate and temperature are higher than expected postoperative levels. In many cases a temperature of only 99° or more has put us on our guard to search for more concrete evidence. If the patient has already experienced pleural pain, dyspnea, cyanosis and possibly hemoptysis, our diagnostic eye is still turned to the lower extremities where the process has likely started. One can corroborate clinical pulmonary embolism with the x-ray and electrocardiogram but confusion may result if the findings are not typical. We wish to emphasize that the diagnosis of leg thrombosis should be made before pulmonary complications ensue. Often too frequently, when lung embolism awakens our interest, it is too late. Robertson showed that out of 149 cases of severe embolism, 39 per cent died within one hour. Many other series present similar figures. The diagnosis of embolism is not always simple as Nygaard has shown. In a study of 289 cases coming to autopsy at the Mayo Clinic, a correct diagnosis was made in 82.35 per cent. Other diagnoses made were coronary occlusion, indeterminate causes, shock and hemorrhage, peritonitis, pulmonary edema, and cerebrovascular accidents. The rationale of such diagnoses can be easily seen.

Since therapy is almost at a loss in handling this complication in its most serious phase, expectant treatment and prophylaxis is all we can offer these individuals. As stated before, a large percentage of these patients die immediately or within a few minutes. The reader is referred to the reports of deTakats and

Nygaard for further statistics. We doubt that the Trendelenburg operation of removal of the clot from the pulmonary artery will ever have a place in any but the occasional case. One wonders in these successful cases whether the patient might not have recovered spontaneously. Nygaard has gone into the impractibility of embolectomy, even in large institutions. Much, however, can be done to prevent this tragedy.

First of all we must become conscious of those patients in whom we feel there is a constitutional background for embolism. This is difficult and rather empirical but a careful history and examination will give significant data in many cases. Emphasis is placed on the presence of varicosities and chronic illness, particularly if there has been a past history of infarction. Next and most important of all we concern ourselves with those patients who do not move freely after their surgery. Any alteration in the pulse or temperature should make us turn our interest to the leg veins for further evidence of impending thrombosis.

Prophylactically there are many things that one can do. Walters advocated thyroid extract daily to promote tachycardia but control figures were not too impressive. We believe that the most effective preventitive measure is early ambulation. If this is not possible, one should at least enforce leg exercises. These may be started as soon as the patient reacts from anesthesia. Motion is also encouraged in the head, arms, and hips as well. The patient should be able to turn himself within 12 hours or sooner. He is frequently assisted to the sitting position without the back rest on the 1st postoperative day and may begin to sit on the edge of the bed by the 2nd day. Ambulation then begins anywhere from the 1st to the 4th postoperative day. In major thoracic operations patients are usually out of bed on the 3rd or 4th day. Statistics would indicate that early ambulation has not had a deleterious effect on wound healing.

If femoral thrombosis develops despite prophylaxis, we may still prevent embolism from occurring. The pendulum of therapy changes abruptly from one of activity now to complete rest to the thrombosed part. Every effort is made to keep the thrombus from dislodging. The leg is elevated to allay venous stasis and efforts are made to incite phlebitis. Heat from a hot water bag or cradle are somewhat effective. Since the advent of the anticoagulants, we have supplementary drugs which can do much. Many operators use heparin and dicumarol prophylactically before thrombosis occurs. Murray and Best cite the use of heparin in 315 patients postoperatively without a single incidence of embolism, while their control series developed this complication in from 2.2 to 7.5 per cent. Again Rehn used anticoagulant therapy

with somewhat stricter indications in a group of 1596 patients. Only 5 (0.32 per cent) developed thrombosis and 1 case embolism (0.15 per cent). The latter case was fatal. In the control group of 1369 where only general preventive measures were used, 26 (2 per cent) developed thrombosis, 17 (1.24 per cent) developed embolism, and 6 (0.44 per cent) died. The disadvantage of such universal use of these drugs lies chiefly in their hemorrhagic tendencies. We believe they are still useful after thrombosis and embolism have occurred. Heparin is begun at once and takes effect promptly by prolonging the clotting time. It is discontinued after the effects of dicumarol are noted. The latter drug has its action on the liver where prothrombin is formed. The normal prothrombin time by Quick's method is 17 to 19 minutes. We usually give an initial dose of 300 milligrams of dicumarol the first day, and from 100 to 200 milligrams the 2nd day. Thereafter, the daily requirement falls abruptly and only 50 milligrams may be needed to maintain the desired prothrombin time of 35 minutes. It has been stated that a prothrombin time of 27 minutes or more will prevent thrombosis, and if it is kept below 60 minutes, hemorrhage will not occur. Daily prothrombin estimates must be made to guide the therapy as a change may occur rapidly. If hemorrhage occurs, prompt use of vitamin K and transfusion of whole blood is helpful in combating it until the prothrombin level falls. Neither heparin or dicumarol will dissolve a thrombus already formed, but they will prevent propogation of the thrombus to a great extent. Anticoagulant therapy is continued until all signs are again normal even to the measurement of the calf.

Homans has stimulated much interest in femoral ligation. There is no one measure which is as surely effective in arresting thrombosis. Many operators advocate bilateral femoral ligation previous to major surgery in debilitated patients, as before prostatic resection and staged cancer surgery. We have taken a middle course and utilized it only after thrombosis has been evidenced. Many patients have been saved from fatality by femoral ligation even after one or more showers of pulmonary embolism have occurred. Priestley found that if secondary emboli occurred, they developed within 10 days in 80 per cent of the patients. When the patient does not make prompt progress after anticoagulant therapy, or if there is any sign of femoral thrombosis, we ligate. Again, if there is any sign of propogation of the clot, we advocate immediate ligation. Ligation is usually done only on the involved side, but we have seen instances where a secondary higher ligation or a contralateral ligation was eventually necessary. The technic of ligation has been well stressed in Homan's work. There should be no hesitancy to ligate the iliac or even inferior vena cava if the

femoral approach does not succeed in removing all proximal clot.

The following case is one of many but it is reported to emphasize some of the salient points of the foregoing discussion.

L.V., a white male, age 22, was admitted to the hospital with a right indirect inguinal hernia which he had noted for 4 months. Only in the last 10 days had it been painful but he was able to keep it reduced at all times. He was in excellent condition and had never been ill enough to be hospitalized before. His height was 68 inches, weight 152 lbs., and muscular development fair to good. He was subjected to a hernia repair under spinal procaine (150 mg.) anesthesia on December 23, 1943. It was noted that he did not move about in the bed too freely after operation and was cautioned about this. His oral temperature by December 27 was still 99.8 degrees F. and the pulse 88. On search for the cause of this low-grade fever, tenderness was elicited in the calf of the left leg. On measurement this leg was 1 centimeter larger than its mate. Dorsiflexion of the foot produced pain in the calf, but the patient did not experience pain unless the leg was moved or the calf muscles gripped. He was not placed on heparin but 300 milligrams of dicumarol was given at once. The leg was elevated and a hot water bag placed on the calf. The initial prothrombin time was 18½ minutes. On the 2nd day, only two 50 milligram doses of dicumarol were given. The prothrombin time was then 25 minutes. Examination of the extremity revealed little change except that the measurement was now 2 centimeters greater than the other calf. By the morning of the 3rd day the patient suffered moderate pleural pain on the right with a mild hemoptysis and slight transient air hunger. This episode lasted but 10 to 15 minutes at most. Examination of the leg now showed tenderness in the left femoral region with little or no change in the calf. Prothrombin time was 38 minutes and the temperature level was elevated over the previous day, the highest reading being 102.4 and the lowest 100.0 degrees F. It was decided to do a femoral ligation at once. Under pontocaine (50 mg.) spinal anesthesia, and in reversed Trendellenburg position, an 8 centimeter longitudinal incision was made over the left saphenofemoral region. The saphenous vein was ligated with fine silk and divided. The femoral sheath was incised inferior to the fossa ovalis and the femoral vein exposed. The vein was somewhat whiter and more thickened than normal. After placing two sutures around the vein loosely, a small opening was made in its wall and no blood flowed. One could see a thrombus lying within the lumen. With a glass-tipped aspirator, the clot was sucked out, bringing with it an elongated pointed free tail which had projected proximally 4 centimeters. Bleeding followed the removal of the thrombus and the ligatures were tied. The vein was then sectioned between additional suture ligatures at this level and the wound closed with interrupted fine silk in layers. Postoperatively dicumarol was continued at its previous level. Temperature receded gradually and was normal by the 3rd day after ligation. He did not have any further pulmonary symptoms nor did he show any hemorrhagic tendencies at the wound sites. Check-up roentgenogram of the chest revealed fairly normal findings. His leg was normal in measurement by the 8th day following ligation. There was no tendency to edema in the dependent position and he experienced no pain or tenderness. He was discharged on his 22nd postoperative day following the hernia repair. Dicumarol was stopped on the 9th day after ligation at which time he was ambulant.

CONCLUSIONS

1) Postoperative pulmonary complications may be infectious, mechanical or circulatory. A review of the most important of these entities has been undertaken, viz. atelectasis, spontaneous pneumothorax and pulmonary embolism.

2) Certain preventive measures will materially lessen the frequency of occurrence of most of the above complications.

3) The treatment of each complication is given briefly. Stress is laid on early recognition of each condition and prompt institution of therapy.

4) Several case reports are related to illustrate a few of the corollaries stressed in this treatise.

CONCLUSIONES

1) Las complicaciones pulmonares postoperatorias pueden ser infecciosas, mecánicas o circulatorias. Se revisan las más importantes de ellas tales como la ateléctasis, el neumotórax espontáneo y la embolia pulmonar.

2) Hay ciertas medidas preventivas que de hecho hacen menos frecuentes las complicaciones antes citadas.

3) El tratamiento de cada complicación se describe brevemente. Se recalca la importancia del descubrimiento temprano y el tratamiento pronto de las complicaciones.

4) Se relatan varios casos para ejemplificar los corolarios sobre cuya importancia se insiste en este trabajo.

REFERENCES

Barker, N. W., Nygaard, K. K., Walters, W. and Priestley, J. T.: "A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism," *Proc. Staff Meet. Mayo Clin.*, 16:1, 1941.

Bartlett, R.: Quoted by E. A. Graham, editor *Year Book of Surgery*, 1945.

Christopher, F. and Shaffer, J. M.: "Postoperative Atelectasis," *Am. J. Surg.*, 32:197, 1936.

Churchill, E. D. and McNeil, D.: "The Reduction of Vital Capacity Following Operation," *Surg. Gyn. and Obst.*, 44:483, 1937.

Cooper, G., Rosenstein, C., Walter, A. and Peizer, L.: "Further Separation of Types Hitherto Included in Group IV and Development of Therapeutic Anti-sera for these Types," *J. Exp. Med.*, 55:531, 1932.

Coryllos, P. N.: "Postoperative Apneumatosis," *J.A.M.A.*, 93:98, 1929.

Coryllos, P. N.: "Postoperative Pulmonary Complications and Bronchial Obstruction," *Surg. Gyn. and Obst.*, 50:795, 1930.

DeTakats, G., Beck, W. C. and Fenn, G. K.: "Pulmonary Embolism," *Surgery*, 6:339, 1939.

Faulkner, W. B. Jr. and Faulkner, E. C.: "Internal Drainage," *Am. J. M. Sc.*, 184:370, 1932.

Galbraith, E. G. and Steinberg, B.: "Developmental Mechanics of Pulmonary Atelectasis," *Ann. Otol., Rhinol. and Laryngol.*, 46:800, 1937.

Goltz: Quoted by DeTakats.

Gray, H. K.: "Postoperative Pulmonary Complications and the Postoperative Use of Trendelenburg Position," *Minn. Med.*, 18:273, 1935.

Haight, C.: "Intratracheal Suction in the Management of Postoperative Pulmonary Complications," *Ann. Surg.*, 107:218, 1938.

Henderson, Y.: "Absorption of Gas," *Arch. Int. Med.*, 49:88, 1932.

Homans, J.: "Venous Thrombosis and Pulmonary Embolism," *New England J. Med.*, 236:196, 1947.

King, D. S.: "Postoperative Pulmonary Complications," *J.A.M.A.*, 100: 21, 1933.

Lee, W. E., Tucker, G. and Clerf, L.: "Postoperative Pulmonary Atelectasis," *Ann. Surg.*, 88:6, 1928.

Lindskog, G. E.: "Studies on the Etiology of Postoperative Pulmonary Complications," *J. Thorac. Surg.*, 10:635, 1941.

Murray, G. D. W. and Best, C. H.: "Use of Heparin in Thrombosis," *Ann. Surg.*, 108:163, 1938.

Myerson, M. C.: "Bronchoscopic Treatment of Lung Abscess," *Surg. Gyn. and Obst.*, 41:573, 1925.

Nygaard, K. K.: "Pulmonary Embolism: Consideration of Clinical Diagnosis and Possibilities for Trendelenburg Operation," *Proc. Staff Meet. Mayo Clin.*, 13:586, 1938.

Overholt, R. H. and Veal, J. R.: "Incidence and Significance of Postoperative Pulmonary Signs," *New England J. Med.*, 208:242, 1933.

Pasteur, W.: "Active Lobar Collapse of the Lung After Abdominal Operations," *Lancet*, 2:1080, 1910.

Phillips, J. R.: "Bilateral Pneumothorax, External Subcutaneous Emphysema Complicating Gastric Resection," *South. Surg.*, 7:188, 1938.

Priestley, J. T., Essex, H. E. and Barker, N. W.: "Use of Heparin in the Prevention and Treatment of Postoperative Thrombosis and Embolism," *Proc. Staff Meet. Mayo Clin.*, 16:60, 1941.

Rehn, E.: "Rational Prevention of Thrombosis to Eliminate Embolism in Surgery," *Deutsch. med. Wchnschr.*, 72:18, 1947.

Robertson, H. E.: "Pulmonary Embolism Following Surgical Operations," *Am. J. Surg.*, 26:15, 1934.

Rolleston, H. D.: "A Case of Fatal Hemopneumothorax," *Clin. Soc. Trans.*, London, 33:90, 1899.

Rovestine, E. A. and Taylor, I. B.: "Postoperative Pulmonary Complications," *Am. J. M. Sc.*, 191:807, 1936.

Scott, H. G. and Ivy, H. C.: "Viscerocardiac Reflexes—An Experimental Study," *Arch. Int. Med.*, 49:227, 1932.

Stephens, H. B.: "A Consideration of Contralateral Pneumothorax as a Complication of Intrathoracic Operations," *J. Thorac. Surg.*, 5:471, 1936.

Takino and Watanabe: Quoted by DeTakats.

Tannenberg, J. and Pinner, M.: "Atelectasis and Bronchiectasis," *J. Thorac. Surg.*, 11:571, 1942.

Walters, W.: "The Suggested Use of Thyroid Extract to Reduce the Incidence of Postoperative Embolism," *Minn. Med.*, 10:25, 1927.

Electrocardiographic Patterns in Pneumothorax*

ROBERT N. ARMEN, M.D. and THOMAS V. FRANK, M.D.
Butler, Pennsylvania

This investigation was stimulated by our observation of certain changes in routine electrocardiograms taken on patients with pulmonary tuberculosis undergoing artificial pneumothorax therapy at this hospital. The study received increased impetus when a definite trend became evident. This consisted of significant EKG differences between the two groups, one receiving right and the other left pneumothorax. While the cardiograms of patients undergoing right-sided pneumothorax did not show a uniform and constant pattern of changes, those of patients receiving left-sided pneumothorax revealed a definite pattern. This difference was seen more predominantly in the chest leads. A review of the literature on this subject disclosed conflicting findings and opinions, which will be discussed subsequently.[1-13]

Method of Study

This study includes 45 male cases, 43 with pulmonary tuberculosis undergoing artificial pneumothorax therapy, one case of spontaneous left-sided pneumothorax and one case of artificial pneumopericardium. Of the artificial pneumothorax group, 20 received right-sided pneumothorax only and with satisfactory collapse of varying degrees; 23 received left-sided pneumothorax only, 20 of which had satisfactory collapse and 3 were reported as unsuccessful. These cases were referred to us routinely from the Tuberculosis Section as soon as a decision for pneumothorax therapy was arrived at. Cases were selected only to the extent that patients with abnormal initial EKG tracings or patients who had already undergone pneumoperitoneum were excluded from the series.

The average age was 28.5 years ranging between 21 and 43. Sixty-two per cent of the cases were in their twenties and only four cases were over thirty-eight. None of the cases in the series had any evidence of heart disease. All but four of the cases reported had EKG tracings taken shortly before the initiation of

*From the Department of Medicine, Veterans Administration Hospital, Butler, Pennsylvania.

Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

collapse therapy. These prepneumothorax cardiograms were all within normal limits. All tracings were taken in the supine position with the three standard limb leads and CF-4. However, in selected cases CF-2 and CF-5 positions were added and in three of the left-sided cases the records were repeated in the standing, right lateral and prone positions, using the same leads. After the initiation of pneumothorax serial tracings were started and continued. The first postpneumothorax tracings were taken as early as the same day in some cases or as long after as one month. In the great majority of cases, however, the first postpneumothorax tracings were taken within three to seven days. Tracings wererepeated at varying intervals and several patients (twelve cases) were followed for a period of six months or longer. The longest period of follow-up in the right-sided group was nine months and in the left-sided group seven and a half months. The case of spontaneous pneumothorax was followed for six months. The case of artificial pneumopericardium was a 22 year old colored male who was being treated in the Tuberculosis Section under a diagnosis of tuberculous pericarditis with effusion. This case is included in the series to compare the effect on electrocardiograms of air in the pleural cavity with that of air in the pericardial sac, as fluid was removed from the pericardial cavity and replaced by air. X-ray films and EKG tracings were taken before and after the injection of air.

Results

I. *The Right-Sided Pneumothorax Group:*

The main electrocardiographic findings were as follows (See Figure II-E):

a) Right axis shift—was seen in eight cases (40 per cent). This group includes six cases in which a definite S wave developed in L-1 and the QRS-1 which was mainly an upright deflection in the prepneumothorax tracing, became a diphasic or equiphasic complex; and two cases in which no S wave developed in L-1 and the QRS-1, which was mainly an upright deflection in the prepneumothorax tracing remained an upright deflection (R) but became much smaller in amplitude—no more than two or at most three millimeters in height.

b) Thus—there were altogether eight cases (40 per cent) with depression of QRS-1.

c) Depression of the P waves in one or more of the limb leads was seen in eleven cases (55 per cent). This was slightly more common in L-1 than in L-2 or L-3.

d) T waves changes—The only T wave abnormality noted was depression or flattening of T-1 in ten cases (50 per cent). There was noted no T inversions or S-T deviations in the limb leads or the chest leads in any of the right-sided cases nor any right heart strain or P-pulmonale patterns.

X-ray plates and fluoroscopic observations of the chest done serially during the course of this study revealed no more than a minor degree of displacement of the heart to the left. However, there was noted no definite correlation between the degree of displacement of the heart to the left and the degree of right axis shift.

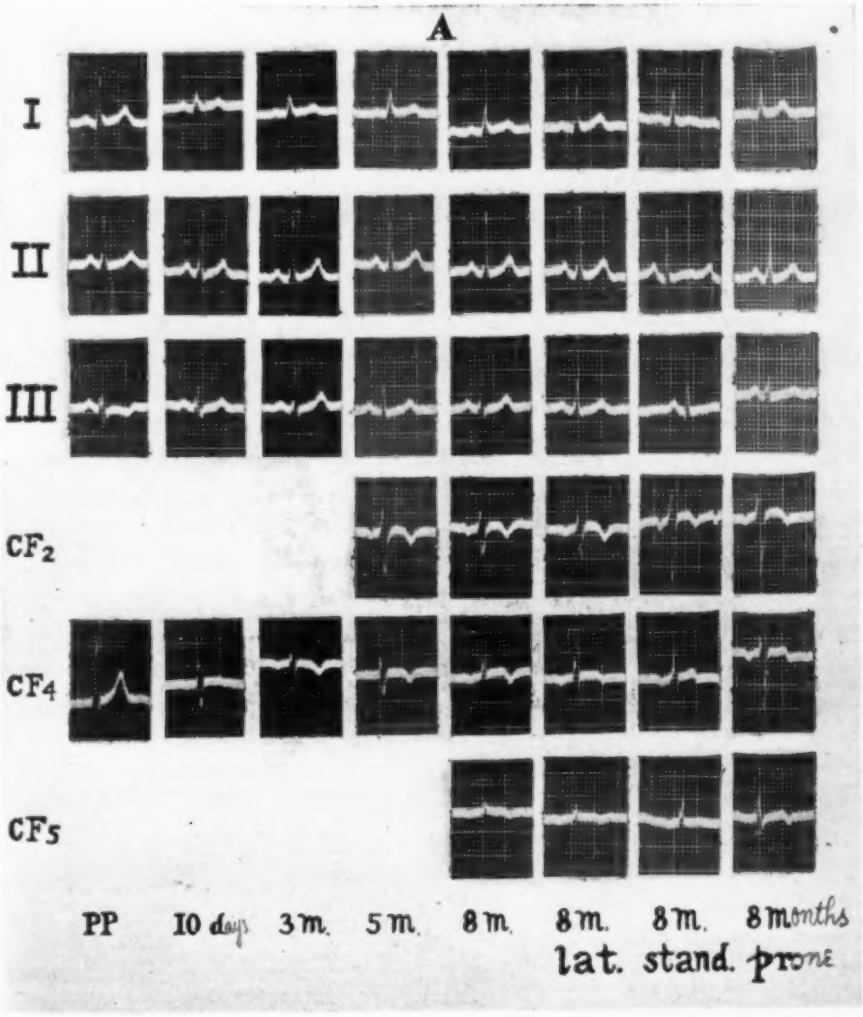


FIGURE I: Case of left-sided pneumothorax; age 26; Leads I, II, III, CF-2, CF-4 and CF5 top to bottom. Columns left to right—PP equals prepneumothorax tracing, and tracings at varying intervals—10 days, 3 months, 5 months, and 8 months. Columns 5 to 8 all taken at 8 months after the initial pneumothorax, in the supine, right lateral, standing and prone positions successively.

II. *The Left-Sided Pneumothorax Group:*

Of the twenty-three cases of artificial left-sided pneumothorax, twenty developed satisfactory collapse. ECG findings in these twenty follows (See Figure I-A):

a) Lowered Voltage of QRS-1:

Lowered voltage of QRS-1 was noted in fourteen cases (70 per cent). This group includes those in which no S wave developed in Lead 1 but the QRS-1, which was an upright deflection in the prepneumothorax tracing, remained an upright deflection (R) but became much smaller in amplitude—no more than 2 or 3 mms. in height.

b) Axis Shift:

There were no cases in which a definite S wave developed in L-1. But, eight cases (40 per cent) showed slight degrees of right axis shift (small R-1, tall R-2 and tall R-3).

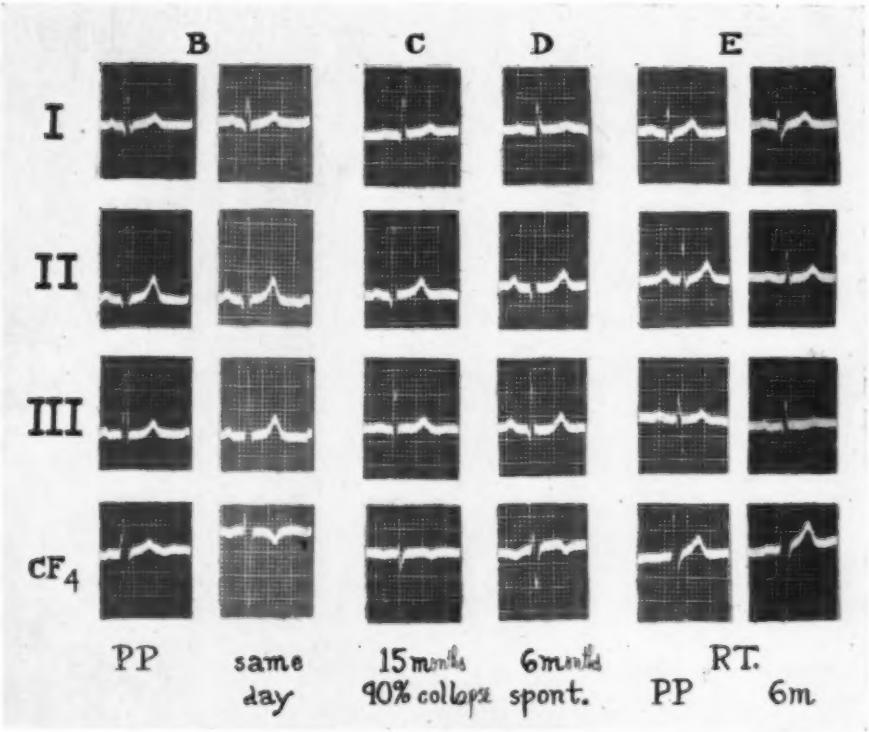


FIGURE II: Leads I, II, III and CF-4 from top to bottom. Columns left to right—Case "B"—left-sided pneumothorax, age 23, PP equals prepneumothorax tracing, and in next column, a tracing taken same day after the initiation of pneumothorax, with 40 per cent collapse. Case "C"—age 21, left-sided pneumothorax; tracing taken at 15 months after initial collapse, with 90 per cent collapse. Case "D"—age 33, left-sided spontaneous pneumothorax of 6 months duration with 75 per cent collapse. Case "E"—right-sided pneumothorax, age 32; PP equals prepneumothorax tracing, and the next column, tracing taken 6 mos. after the initial pneumothorax, with 60 per cent collapse.

Left axis shift was not seen in any of the cases reported. Displacement of the heart to the right was noted in eleven of the cases but in only minor degrees. Again, no correlation was noted between the amount of displacement and the degree of axis shift.

c) Depression of P waves:

Depression of P-1 was seen in only four cases (20 per cent).

d) T-changes in the Limb Leads:

Thirteen cases (65 per cent) showed a lowered voltage or flattening of T-1 so that T-3s were thereby larger than T-1s.

e) P-R and QRS Intervals:

There were no cases of prolonged P-R or QRS interval and no definite pattern of S-T deviation in the limb leads.

f) T changes in Chest Leads:

All of the twenty cases (100 per cent) had T wave changes in one or more of the chest leads. These consisted of definite T wave inversions in all but one case. In the latter the T waves were merely flattened. The inverted Ts were peaked, symmetrical and with smooth shoulders bowed upward, thus resembling typical coronary T waves, and with S-T-T contour also of the coronary type (See Figure I-A, CF-4 in Column III-M).

g) Contour of QRS in Chest Leads:

There was noted a definite change in the contour of QRS complexes in the chest leads. Nineteen of the twenty cases (95 per cent) had definite depression of R-4 to below 3 mm. in amplitude. Twelve cases (60 per cent) developed prominent S waves in CF-4 which were absent or no more than 3 mm. initially. In two cases the R waves were completely lost and QS waves became prominent. Six cases showed a lowering of voltage of both the R and S waves.

In twelve cases (60 per cent) multiple chest leads were taken, CF-2, CF-4, CF-5, once or twice during the course of the follow-up. In ten of the twelve cases the T waves in CF-2 and CF-5 were inverted together with those in CF-4, with the T wave inversions in CF-2 being more marked than in the other leads; while the QRS irregularities, especially that of lowered voltage, was more pronounced in CF-4 and CF-5 than in CF-2. Actually, the trend was towards more abnormal T waves in the right-sided leads and more abnormal QRS waves in the left-sided leads (Fig. I-A).

The tracings in three cases of the left-sided pneumothorax group were repeated in various other positions than supine, such as, right lateral, standing, and prone, for comparison with tracings taken in the supine position. With this short series of three cases,

it is impossible to establish a trend, however, so much can be stated that regardless of the position used, T wave inversions were present in one or another of the three chest leads used (See Figure I-A, last 3 columns), although in the prone position the T wave inversions were the least marked and T waves were nearer to normal than in any other position. Littman,[8] and Feldman and Silverberg[2] state that the T wave inversions disappear in all other positions but the supine. Actually, in one of the three cases, the upright T waves in CF-2 taken in the supine position became moderately inverted in the prone position.

The three cases of left-sided pneumothorax classified as unsuccessful (no demonstrable collapse), showed no appreciable ECG changes.

The case of spontaneous pneumothorax (left) was followed for a period of six months. The initial T changes in the chest Leads were comparable to those found in patients undergoing left artificial pneumothorax. After six months follow-up the spontaneous pneumothorax persisted in spite of therapeutic attempts to obliterate the pleural cavity and thus re-expand the lung. The T wave inversions continued to be present although not to as marked a degree as was seen initially (Figure II-D).

In the one case of pneumopericardium, no appreciable difference was noted between the two electrocardiographic tracings taken just with fluid in the sac and then with air in the sac (See Figures III-B and A).

Discussion

Abnormal ECG patterns have been noted in patients receiving pneumothorax therapy and have been discussed many times in the literature.[1-13] However, the striking differences in ECG pat-

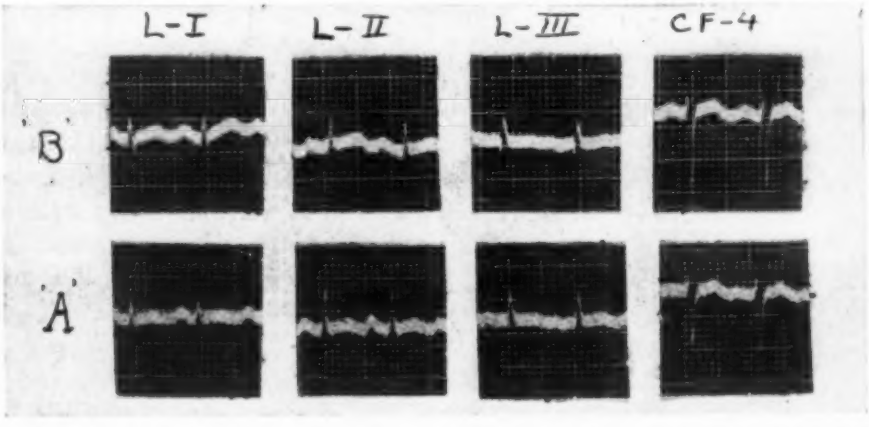


FIGURE III: ECG—Leads I, II, III and CF-4—from left to right. "B"—tracing taken with fluid in pericardial sac. "A"—tracing taken with air in pericardial sac.

terns between right and left pneumothorax were not clearly demonstrated until comparatively recently. Then Miller,[11] in 1945, reported a series of cases all with left pneumothorax and "mediastinal emphysema," demonstrating a pattern with low T waves in Lead-1, and flat or inverted T waves, elevated S-T segments and small or absent R waves in the 4th Lead. Littman,[8] in a short series, more or less supported Miller's previous observations but pointed out that these abnormal findings were present only in the supine position. He concluded that the ECG alterations were the result of the presence of air between the heart and the exploring electrode. Previous to this it had been suggested that the ECG changes were due to an alteration in the coronary circulation.[12] Still other investigators, notably Goldberger and Schwartz,[4] believed that the rotation of the heart about one or more of its three axes could account for the ECG alterations which they noted in cases of pulmonary tuberculosis with collapse. More recently, Feldman and Silverberg,[2] concluded that these ECG changes in left-sided pneumothorax were due to a combination of displacement of the heart and interposition of air between the heart and the chest wall.

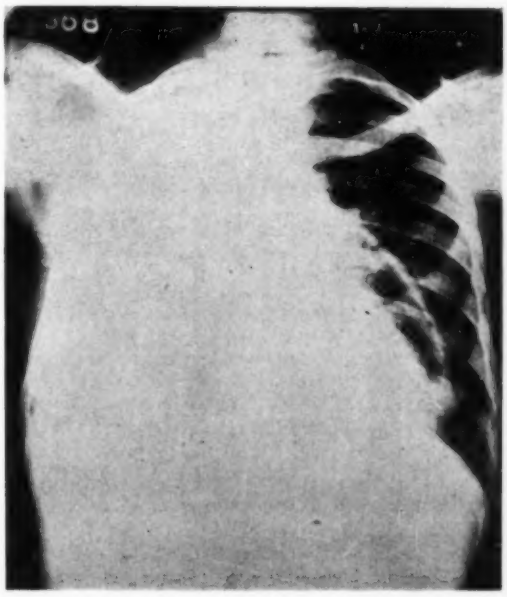


FIGURE IV: Case of tuberculous pericarditis, age 22. X-ray film of chest in P-A.

In our series we have shown a definite pattern of ECG changes in the left-sided pneumothorax group. The most conspicuous of these changes are the T inversions in the chest leads which occurred in all but one of our reported cases. In the right-sided

cases, these T inversions are notably absent, and the only abnormal pattern has been a tendency to right axis shift and depression of the P waves in the limb leads. In the left-sided group, the T wave inversions, as well as the other changes, have appeared as early as the same day of collapse in many cases (Figure II-B), while in others, there has been a gradual depression of the T waves with eventual inversion in a course of days or weeks (Figure I). In the majority of cases the QRS depression both in Lead 1 and in CF-4 has appeared earlier than the T inversion. With the exception of three cases, all T wave changes have persisted to the end of this study. In these three cases the T inversions reverted to normal and remained normal in spite of the presence of air in the pleural cavity and maintenance of satisfactory collapse. We are unable to state at this time how long these changes

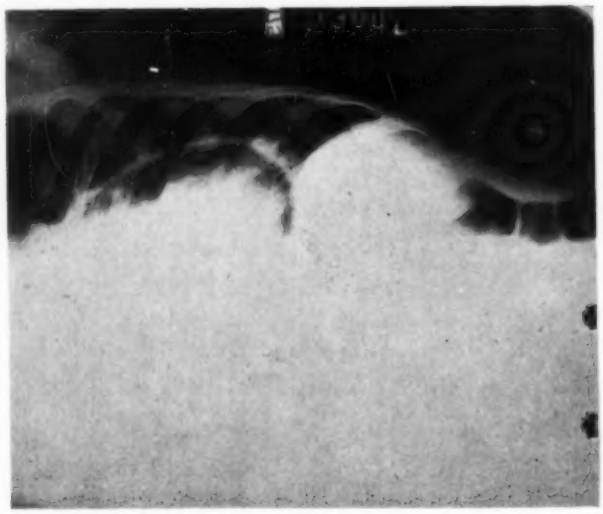


FIGURE V: Same case as in figure 4, in a right-sided lateral decubitus position; taken after fluid was aspirated and air injected into the pericardial sac.

will tend to persist. However, one case that was observed fifteen months after the initiation of pneumothorax still maintained the characteristic changes in CF-4 (Figure II-C). Thus, it might be assumed that these changes may persist as long as the pneumothorax is maintained. Our findings differ from those of Littman,[8] and others,[2] concerning the disappearance of the T inversions in other positions than supine. We have shown such T inversions in one or more chest leads in other positions than supine, i.e., in right lateral, standing and prone (Figure I). The T inversions are most conspicuous in the supine position and least so in the prone.

It is interesting to note that the shift of electrical axis when

it occurs is always to the right, regardless of the side of the chest undergoing pneumothorax. We have found this axis shift to the right to be more common in right than in left pneumothorax. This finding is comparable with that of Treiger and Lundy.[13] We have seen no definite correlation between the amount of heart displacement and the degree of axis shift, and no correlation whatsoever between the percentage of collapse and the degree of T inversion or any of the other changes described. This is very well demonstrated in Figure II, in cases B and C where the T inversion in case C with 90 per cent collapse is much less striking than in B with only forty per cent collapse. In the one case of spontaneous left-sided pneumothorax the changes are comparable with those in artificial left-sided pneumothorax (Figure II-D). However, Master,[10] expresses the opinion that the changes in spontaneous pneumothorax are usually more marked than those in artificial cases.

As for the causes effecting these changes, it seems likely that a combination of factors are at work. The fact that these abnormal T waves resemble coronary T waves have suggested to some authors the possibility of changes in the coronary circulation.[8,12] The lack of clinical evidence of coronary disease or insufficiency as well as the lack of other coronary ECG patterns make this hypothesis unlikely. We believe that displacement of the heart *alone* is also an unlikely factor, as regardless of the direction of the displacement of the heart the electrical axis shift always happens to be to the right. Also, in spite of the presence of displacement and axis shift, we were unable to show T inversions in the right-sided cases. A more plausible factor, we believe, is the presence of air in the pleural cavity situated between the heart and the chest wall and acting as a poor conductor.[7,8] Considerable evidence is present to support this hypothesis although not conclusive: the fact that the T inversions are found only in the left-sided cases; and the fact that these T inversions are absent or much less striking in cases of left-sided collapse effected by left-sided thoracoplasty. However, there are several undeniable arguments against the air hypothesis: (1) There is no correlation between the percentage of collapse and the degree of T inversion. (2) T changes persist in other positions than supine, such as in right lateral, standing and prone, although not to as striking a degree as in supine. (3) In three cases in our series the inverted T wave reverted to normal in spite of the maintenance of collapse and continued presence of air in the pleural cavity. (4) In the one case of pneumopericardium reported the ECG pattern was similar before and after the introduction of air into the pericardial sac (Figure III). It would be reasonable to assume that an amount

of air (100 cc.) in a smaller cavity, namely the pericardial sac, would be more effective or at least as effective in bringing about such ECG changes as are observed when air is present in the pleural cavity, a much larger space. We believe that probably rotation of the heart rather than displacement is another factor to be considered, and that both rotation and air as well as other unknown factors working in combination might be responsible for these changes.

SUMMARY

1) Forty-five cases have been presented; forty-four with pneumothorax of one or the other side, and one with artificial pneumopericardium, with serial electrocardiographic studies before and after the initiation of pneumothorax or pneumopericardium.

2) Characteristic ECG patterns both in right and left sided pneumothorax have been shown and described.

3) A marked and definite difference in these ECG patterns between the right and left sided groups has been shown and illustrated.

4) The ECG pattern in the right sided group has been mainly a tendency to right axis shift, depression of QRS-1, and depression of P waves in the limb leads. T inversion has been notably absent.

5) The ECG pattern in the left sided group has been more conspicuous and more striking, and has consisted of a lower voltage of QRS-1, flattening of T waves in Lead 1, a change in the contour of QRS complexes in the chest leads, and a definite inversion of T waves in the chest leads; these T wave inversions being the most constant and conspicuous of all changes.

6) The T wave inversions have persisted in various other positions than supine, namely, standing, right lateral and prone.

7) As for the basic cause effecting these changes, the evidence is not conclusive. However, available evidence points to rotation of the heart and the presence of air between the heart and the chest wall as very probable causative factors.

Note: We wish to express our thanks and gratitude to Doctors George C. Glinsky, A. C. Cohen, and L. H. Hetherington for their generous help and suggestions during the course of this study.

RESUMEN

1) Se han presentado cuarenta y cinco casos; cuarenta y cuatro con neumotórax de uno o el otro lado y uno con neumopericardio artificial, con estudios electrocardiográficos seriados antes y después de iniciar el neumotórax o el neumopericardio.

2) Se han demostrado y descrito patrones electrocardiográficos

característicos, tanto del neumotórax del lado derecho como del izquierdo.

3) Se han demostrado e ilustrado decididas y bien definidas diferencias en estos patrones electrocardiográficos entre los grupos del lado derecho y del izquierdo.

4) El patrón ECG en el grupo del lado derecho ha sido principalmente una tendencia a desviación del eje derecho, depresión de QRS-1 y depresión de las ondas P en las conexiones de las extremidades. Ha sido notable la ausencia de la inversión de T.

5) El patrón ECG en el grupo del lado izquierdo ha sido más conspícuo y más notable, y ha consistido de voltaje más bajo de QRS-1, aplastamiento de las ondas T en la conexión 1, un cambio en el contorno de los complejos QRS en las conexiones del tórax y una inversión bien definida de las ondas T en las conexiones del tórax; la inversión de estas ondas T ha sido el más constante y conspícuo de todos los cambios.

6) Las inversiones de las ondas T han persistido en otras posiciones además de la boca arriba, a saber, de pies, lateral derecha y boca abajo.

7) No se ha determinado conclusivamente la causa fundamental que influencia estos cambios. Sin embargo, las pruebas asequibles indican que la rotación del corazón y la presencia de aire entre el corazón y la pared torácica probablemente son los factores causales.

REFERENCES

1 Anderson, A. R.: "EKG Studies in Artificial Pneumothorax and Thoracoplasty," *Am. Rev. Tuberc.*, 20:728, 1929.
2 Feldman, D. and Silverberg, C.: "Electrocardiographic Changes in Pulmonary Collapse Therapy," *Am. Heart J.*, 35:800, 1948.
3 Fox, T. T. and Kremer, H. S.: "Heart in Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 47:135, 1943.
4 Goldberger, E and Schwartz, S. P.: "EKG's in Chronic Pulmonary Disease," *Am. Rev. Tuberc.*, 53:34, 1946.
5 Hansen, O. S. and King, F. W.: "Influence of Pulmonary Collapse on the Electrocardiogram," *Am. Rev. Tuberc.*, 22:320, 1930.
6 King, F. W. and Hansen, O. S.: "Electrocardiographic and Roentgenographic Studies of the Heart in Tuberculosis," *Am. Rev. Tuberc.*, 22: 310, 1930.
7 Levinson, J. P., Caldwell, D. M., Hetherington, L. H. and Marcy, C. H.: "Studies of Venous Pressure, Vital Capacity, Circulation Time and Electrocardiograms in the Course of Pulmonary Collapse Therapy," *Dis. of Chest*, 14:19, 1948.
8 Littmann, D.: "Electrocardiographic Phenomena Associated with Spontaneous Pneumothorax and Mediastinal Emphysema," *Am. J. M. Sc.*, 212:682, 1946.
9 Lorge, H. J.: "Electrocardiography in Tuberculous Patients," *Am. Rev. Tuberc.*, 45:528, 1942.
10 Master, A. M.: "Electrocardiographic Changes in Pneumothorax in which the Heart has been Rotated," *Am. Heart J.*, 3:472, 1928.
11 Miller, H.: "Spontaneous Mediastinal Emphysema with Pneumothorax Simulating Organic Heart Disease," *Am. J. M. Sc.*, 209:211, 1945.
12 Simon, S and Baum, F.: "Electrocardiographic Studies in Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 17:159, 1928.
13 Treiger, I and Lundy, C. J.: "Correlation of Shifting Electrical Axis of the Heart with X-ray Observations in Artificial Pneumothorax," *Am. Rev. Tuberc.*, 29:546, 1934.

Abstract of Replies to a Questionnaire on Intrapleural Artificial Pneumothorax*

EDWARD W. HAYES, M.D., F.C.C.P.
Monrovia, California

To obtain the present opinions on pneumothorax, a questionnaire was sent to a number of physicians who have been working in this field for a long time and have, with few exceptions, been engaged in teaching. Questions bearing on pneumothorax, other than the length of time it should be continued under different conditions, were asked.

These questions were: (1) In what percentage of patients is pneumothorax now employed? (2) How long is successful pneumothorax continued, (a) in cases with cavitation, (b) in others? (3) Is pneumothorax used as an adjunct to the rest regimen? (4) If so, are patients given a three to six months period of rest, to determine if their disease will come under control, before the institution of pneumothorax? (5) When pneumothorax is instituted, are patients kept at rest for a prolonged period—a minimum of six months? (6) Are patients treated with ambulatory pneumothorax, that is, without having more than a few weeks of bed rest following the induction of the pneumothorax?

There were 90 replies. Many physicians manifested considerable interest by writing at some length. A few gave indefinite answers which could not be classified. Some stated that they wished to know the optimal time to discontinue a successful pneumothorax. These men asked to be informed of any conclusion drawn from this survey.

There was no unanimity of opinion in the replies to any of the questions. The proportion of the patients, under the care of the interrogated group of physicians, on whom pneumothorax is established or on whom an attempt is made to establish pneumothorax varies from 4 per cent to 100 per cent.

A Saranac Lake physician whom, incidentally, I saw give the first pneumothorax I had ever witnessed 30 years ago this summer, said he believed that in the last 10 years we have come to the realization that pneumothorax, in the long range view, is a dangerous procedure and that the whole subject needs periodic going over and re-evaluation.

---

*Round Table Discussion, 14th Annual Meeting of the American College of Chest Physicians, Chicago, Illinois, June 20, 1948.

Eight of the physicians said they are using pneumothorax in 10 per cent of their patients. This was the greatest number of men employing pneumothorax in the same percentage of patients. One physician who has been treating tuberculous patients for more than 30 years replied that he now uses pneumothorax in only 10 per cent of his cases where ten years ago he employed it in 35 per cent. He said that all of his coleagues at Saranac Lake as well as most physicians in the East, are using pneumothorax less frequently than in former years. They are trying to avoid tuberculous empyema which 15 to 25 years ago occurred in 16 to 18 per cent of their pneumothorax cases. They believe a high proportion of empyema is avoided by using pneumothorax in early cases and not in those with more advanced disease with peripheral involvement. One physician reported only one case of empyema complicating pneumothorax in the past four and one-half years. He thought this was due to better management of patients. The one occurred in an un-cooperative patient.

The reason given in general for the present less frequent use of pneumothorax is to avoid complications. Apparently more physicians are offering patients an opportunity to overcome their disease on the rest regimen without instituting pneumothorax, or at least before it is established. This course is followed with an appreciation of the meaning of rest as it applies to a patient with tuberculosis as well as an understanding of its limitations. It also appears that instead of the more indiscriminate use of pneumothorax there is a more frequent use of paralysis of the diaphragm, pneumoperitoneum, primary thoracoplasty and primary resection and, more recently, the use of streptomycin in carefully selected cases. Primary thoracoplasty apparently is being used more frequently in patients especially past middle life and particularly where the disease is limited, for the most part, to a cavity in the apex. There also appears to be a fairly general feeling that where the upper lobe is largely destroyed by the disease and where there is involvement of the larger bronchi, other conditions permitting, primary thoracoplasty and at times primary resection offer the best possibility for the permanent control of the tuberculous.

One physician regarded pneumothorax to be a valuable type of treatment if properly handled but he felt that it is frequently abused and mishandled and blamed for much of the operators' shortcomings and lack of experience. Another believed that each patient is a case unto itself and should be cared for as an individual, not by mass therapy. One with more than 30 years of experience, stated that he employs pneumothorax regardless of the stage of the disease in every patient on whom it could be

established. He apparently tries pneumothorax on all patients. Other opinions varied between these extremes. The opinion was expressed that indications for the use of pneumothorax and for its termination, as well as for all the other phases of treatment, must be based on a clear concept of the pathogenesis of tuberculosis as well as on the knowledge of the pathological physiology in any particular case. In emphasizing the importance of rest in treatment, this physician said pneumothorax does not influence the basic reaction between the invading organism and the cellular reaction of the host.

A physician working in one of the oldest institutions in the New England area wrote that he starts pneumothorax at once in the following cases: (a) Those with a cavity over 2 centimeters in diameter. (b) Those with large cavities which are not of the tension type. (c) Those with smaller cavities with recent spread of disease in the same lung. (d) Those with involvement which exceeds more than a third of the lung and is of the honeycomb or the ulcero-exudative type. (e) Those with unilateral disease who have hemoptysis of more than two tablespoons of bright red blood not controlled otherwise. (f) In the above cases the patients must be between 12 and 50 years of age; the function of the heart good; the vital capacity not less than half its normal amount (judging by estimation of the diaphragmatic movement by fluoroscopic examination) and absence of emphysema and an acute stage of asthma. This physician stated that ambulatory pneumothorax is used in many patients.

The time element in pneumothorax is reckoned from closure of cavities and/or sputum conversion.

In discussing the duration of pneumothorax, one physician commented: "Individualization is the basic factor, generally speaking, in determining how long pneumothorax should be continued." A number of physicians said the termination depended upon many factors, such as the size, complexity and location of the cavitation, the thickness or thinness of the cavity walls, the amount of additional parenchymal disease, the effectiveness of the pneumothorax, presence or absence of complications and associated bronchial disease, etc. One physician stated that under certain conditions pneumothorax should be continued for life, but he did not specify the conditions.

A physician who was among the first to use pneumothorax in tuberculosis in this country, said that after three years, in cavity cases, he allows the lung to expand slowly. If there are signs that the cavity is not closed or there is recurrence or increase of cough and expectoration, the pneumothorax is continued for another year or more. Then another attempt is made to let the lung expand.

Another physician replied that more recently he has been terminating pneumothorax after shorter intervals than formerly in order to avoid pleural complications that are always a threat as long as pneumothorax is present. However, he felt that in the past, expansion was often allowed to take place too soon because of the absence of planigrams and gastric lavage which now make more accurate observations possible. This same physician believes that if pneumothorax does not accomplish its purpose in two or three years, thoracoplasty is needed to prevent relapse.

Most of those commenting on the time element of pneumothorax directed their remarks to the handling of cavity cases. There were four or five physicians who stated that they did not use pneumothorax in the absence of cavitation. One said that unsuccessful pneumothoraces are many times carried on too long, and that the indiscriminate continuation of successful pneumothorax on a time basis without knowledge of or regard for the original condition as an indication should be condemned. One physician said that there is nothing so important as the judgment to determine when pneumothorax should be terminated.

The majority of physicians stated that they use pneumothorax only as a supplement to the rest regimen. The larger proportion stated that unless there are specific indications why pneumothorax should be established without a prolonged delay, they prefer to have their patients experience a period of three to six months rest. This, in general, meant what is ordinarily termed "typhoid rest." These men were of the opinion that a fairly large proportion of patients that have an opportunity to carry out rest in its true sense, especially during the early or acute stage of their disease, will overcome their disease in a reasonable length of time without the use of mechanical therapy.

The majority of physicians were not in favor of ambulatory pneumothorax, that is, instituting the treatment under conditions where the patient is either not put to bed at all or for only a few weeks. Many physicians who oppose this type of treatment expressed their feelings by such answers as "absolutely not;" "definitely no;" and one man in a position to observe end results from many sources asked the question, "Is that treatment?" One man stated, "Mere collapse of the lung does not mean that the lung is healed—healing will occur more rapidly and more surely if the collapse is carried out in connection with the rest regimen and there will be fewer complications." Another stated that he, "looks upon tuberculosis as a generalized disease and believes that in its treatment rest for the body as a whole is the important factor." One physician commented in referring to ambulatory pneumothorax, "You are asking for trouble if it is done very often."

The majority of physicians who use ambulatory pneumothorax stated that they carry out this type of treatment only under unusual circumstances, such as where facilities for bed rest are not available. One replied, "I have many cases under ambulatory pneumothorax treatment. Most of my cases are started in general hospitals and it is almost a practical necessity to use ambulatory pneumothorax treatment because I am not able to keep the patient in the general hospital any length of time." Another said that he used ambulatory pneumothorax quite extensively and stated, "I am beginning to believe this is a justifiable form of treatment." Another physicians who stated that he institutes pneumothorax in his office and if necessary sends patients home in an ambulance, said that he was of the opinion that criticism of ambulatory pneumothorax is definitely unwarranted.

It appears from the answers to these questions that there is a tendency to use pneumothorax less frequently in the treatment of pulmonary tuberculosis, primarily because of the hazards pneumothorax involves. There appears also to be some increase in the use of other forms of mechanical therapy which, at times at least, supplant pneumothorax. It seems evident, too, that, in general, rest in its more comprehensive meaning is being recognized more and more as the basic factor in the treatment of pulmonary tuberculosis. Twenty-five years ago, Allen Krause wrote that rest alone had returned thousands of individuals to health and a productive life. More recently, Max Pinner wrote that "the very foundation of all treatment of active pulmonary tuberculosis is rest" and continuing he said, "How highly the therapist estimates the therapeutic efficiency of rest depends largely upon his willingness to give it a complete and thorough trial over a sufficiently long period of time and on his clear recognition of the limitations of a pure rest regimen." He then pointed out that just being in bed does not constitute bed rest for the tuberculous patient. True rest for the tuberculous is secured only by the physician's psychological control of the patient—a control made possible only by the physician taking the patient into his confidence and explaining to him his disease as well as the cure with all its intricacies and by providing an environment that is conducive to his adjustment to the cure.

Finally, in evaluating the effectiveness of any phase of the treatment of pulmonary tuberculosis it is essential to bear in mind that a certain proportion of patients, estimated to be about one out of every four, will overcome their disease without treatment or regardless of treatment. They are the patients with the resolving type of pulmonary tuberculosis. Unfortunately, at the outset it is not possible to determine which patients will and which

patients will not need treatment. They must all be treated with judgment and caution until the course of their disease is definitely evident. When the possibility of the spontaneous recovery from tuberculosis is not taken into consideration, conclusions as to the value of certain factors in treatment may be misleading.

Number of Physicians	Percentage of Patients Given Pneumothorax	Number of Physicians	Number Years Pneumothorax Given in Cavity Cases	Number of Physicians	Number Years Pneumothorax Given in Cases Without Cavity
1	4	1	1½-3 yrs.	1	½-1 yr.
4	5	4	2 yrs.	1	½-3 yrs.
8	10	4	2-3 yrs.	1	1 yr.
3	15	1	2-4 yrs.	3	1-1½ yrs.
1	15-25	4	2-5 yrs.	8	1-2 yrs.
6	20	2	2½-3 yrs.	4	1-3 yrs.
2	20-25	8	3 yrs.	15	2 yrs.
4	25	10	3-4 yrs.	8	2-3 yrs.
7	30	12	2-5 yrs.	6	2-4 yrs.
2	30-35	4	3-6 yrs.	11	3 yrs.
1	30-40	3	3½-5 yrs.	5	3-4 yrs.
6	35	5	4 yrs.	4	3-5 yrs.
2	40	6	4-5 yrs.	1	5 yrs.
7	50	11	5 yrs.		
6	60	1	5-8 yrs.		
1	65	1	7+ yrs.		
2	70	1	Indefinitely		
2	75				
1	85				
1	90				
2	95				
1	100				

Answers to Question No. III	Yes 62	No 17
Answers to Question No. IV	Yes 48	No 29
Answers to Question No. V	Yes 59	No 21
Answers to Question No. VI	Yes 11	No 50
Ambulatory Pneumothorax Given Only Under Unusual Circumstances		18

13 physicians out of 70 use pneumothorax in 10 per cent or less of their patients.
29 physicians out of 70 use pneumothorax in 25 per cent or less of their patients.
45 physicians out of 70 use pneumothorax in 35 per cent or less of their patients.
54 physicians out of 70 use pneumothorax in 50 per cent or less of their patients.
24 physicians out of 78 continue successful pneumothorax for 3 years or less in cavity cases.
33 physicians out of 68 continue successful pneumothorax for 2 years or less in cases without apparent cavitation.

Treatment of Aortic Aneurysms by Wrapping with Foreign Body*

J. K. POPPE, M.D., F.C.C.P.
Portland, Oregon

The distorted anatomy, invasive tendencies, large size, and friable thin walls of both syphilitic and arteriosclerotic aortic aneurysms contraindicate any attempt at extensive surgical manipulation in the form of resections and anastomoses of these aneurysms. The pounding, pulsating pressure exerted by these aortic dilatations presents an almost malignant tendency to invade and penetrate any adjacent soft tissue. Even the walls of the bony thorax can be eroded by an expanding pulsating aneurysm.

The intense foreign body reaction produced by cellophane and impure polythene film with its constricting fibrosis seems to offer the simplest and most satisfactory method of at least curbing the expansion of these aneurysmal dilatations. This possibility was suggested by the report of Harrison and Chandy[1] who had gradually eliminated two arteriovenous aneurysms of the subclavian vessels by cellophane. Harrison's clinical application of the material resulted from the report of Pearse,[2] who had demonstrated the ability of cellophane to produce gradual obliteration of the lumen of important blood vessels, such as the internal carotid, in the place of the previously devised and somewhat unsatisfactory clamps and bands. This constricting property of cellophane had been demonstrated originally by Page,[3] who used it in 1939 to produce artificial nephritis and hypertension in dogs by wrapping it around the kidneys.

A dilemma arose, however, from the reports of McKeever[4] and others that cellophane produced no reaction and was suitable for reconstructing tendon sheaths and lining joint spaces. An experimental study was undertaken at Washington University School of Medicine with several chemically different varieties of cellophane and plastic material, supplied through the courtesy of the DuPont de Nemours Company of Wilmington, Delaware. The results of this investigation published in greater detail elsewhere,[5] suggested that a new impure plastic known as Polythene film produced the most intense foreign body reaction, whereas some of the other types produced little if any reaction. This fibrotic

*Presented at the 14th Annual Meeting, American College of Chest Physicians, Chicago, Illinois, June 20, 1948.

reaction produced by the impure polythene film was somewhat surprising since it was supposed to have been chemically inert. Considerable confusion has arisen during the past year since Ingraham, Alexander and Matson[6] reported pure polythene especially refined for medical use to be physiologically inert and suitable for covering exposed brain tissue. This was not the result observed by Renault and myself in our animal experiments with impure polythene film supplied by the DuPont Company (Figs. 1, 2 and 3). Hasty comparison of results with other experimental research workers in various parts of the country indicated that four other groups had obtained definite scar tissue formation from the use of impure polythene film obtained from the DuPont Company. Several others are still carrying on animal experiments but do not have their final results available as yet. Yaeger and Cowley[7] recently reported their experimental results at the American Surgical Association Convention in Quebec in which the contaminant dicetyl phosphate present in the DuPont polythene film was found to be the irritating factor. It is hoped that polythene film with an even greater percentage of dicetyl phosphate can be obtained for further experimental work to create a more intense reaction and fibrosis.

Impure polythene film was selected, therefore, to wrap aneurysms of the thoracic aorta to induce an intense foreign body fibrous tissue reaction around the aneurysm, thereby preventing its further expansion and rupture.

Operative Technique

The patient is placed on the side opposite the aneurysmal dilatation of the thoracic aorta using endotracheal ether and oxygen. Through a para vertebral incision extending around the angle of the scapula, the entire length of the fifth or sixth rib is resected and the pleura opened through the bed of the resected rib. The lung is retracted and the mediastinal pleura dissected free from the aneurysm, exposing as much of the surface of the diseased aorta as can be safely freed without danger of rupture. It is frequently impossible to free the entire circumference of the descending aorta because of beginning erosion of the vertebrae and ribs around the origins of the intercostal vessels. The pleura may be too attenuated and adherent over the thin bulging areas to permit its complete removal. A sheet of impure polythene film is then cut to fit the dilated portion of aorta without extending over adjacent normal structures. This film is then sutured loosely to any suitable mediastinal tissue with fine silk sutures, care being taken not to pass any sutures directly into the wall of the aneurysm.

One other saccular aneurysm of the ascending aorta was ex-

SUMMARY OF RESULTS

Polythene film was used to wrap or patch the nine syphilitic aneurysms of the thoracic aorta reported below.

No.	Name	Place	Place	Type	Location	Symptoms	Result
1.	W.W.	7/ 6/45	Barnes Hosp., St. Louis, Mo.	Fusiform	Descending aorta	Pain anterior and posterior chest	Complete relief of pain 1 yr. later
2.	L.P.	10/11/45	Colored City Hosp., St. Louis, Mo.	Saccular	Ascending aorta	Pain anterior chest and weakness	Cannot be traced, believed dead
3.	J.E.	12/ 8/45	Barnes Hosp., St. Louis, Mo.	Saccular and fusiform	Ascending aorta and innominate	Chest pain and weakness	Relief of pain but tires easily
4.	D.H.	1/ 2/46	White City Hosp., St. Louis, Mo.	Saccular	Ascending aorta	Cough and pain anterior chest	Cannot be traced, believed dead
5.	F.K.	11/29/46	Good Samaritan Hosp., Portland, Oregon	Fusiform	Descending aorta	Cough and chest pain	Relief of chest pain, died, hemorrhage esophagus 1½ yrs. later
6.	W.H.	1/16/47	Veterans' Hosp., Portland, Oregon	Fusiform	Distal arch and descending aorta	Chest pain	Relief of pain
7.	J.L.	6/28/47	County Hosp., Portland, Oregon	Fusiform	Distal arch and descending aorta	Chest pain, chronic cough, Hemoptyses and dyspnoea	Died, hemoptysis
8.	C.E.	7/10/47	Veterans' Hosp., Portland, Oregon	Saccular and fusiform	Ascending aorta	Anginoid pain on exertion	Moderate relief of pain, increased exercise tolerance
9.	A.J.	9/22/47	St. Vincents Hosp., Portland, Oregon	Saccular and fusiform	Distal arch	Posterior chest pain and dysphagia	Died, hemorrhage 3 months later

plored at the Portland Veterans' Hospital but found unsuitable for wrapping due to erosion of the anterior chest wall and inability to dissect away the superior vena cava which was imbedded in the aneurysm wall. Several other patients have been considered unsuitable for surgery either because of severe cardiac decompensation or obstruction of the left main bronchus by pressure from the aneurysms.

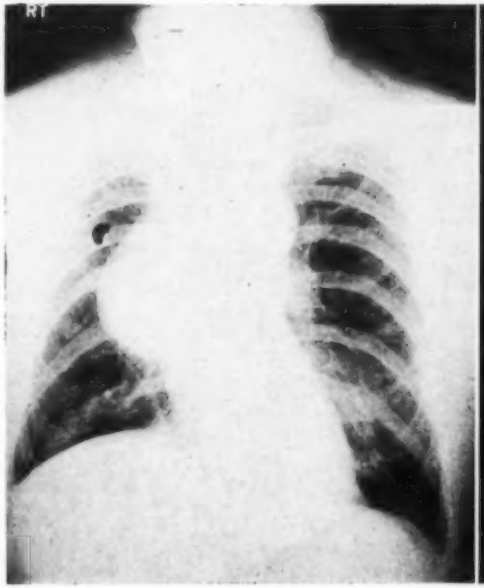
Four of the nine patients whose aneurysms were reinforced by polythene have already survived from one to three years with moderate to complete relief of symptoms of pain in all cases. A period of from three to six months was required to obtain maximum benefit in most patients. Little if any improvement has been noted in strength, although the relief of pain has permitted one patient to return to full time employment and the other three to increase their activities. The patient who died of rupture of his aneurysm into the esophagus one and one half years after wrapping had obtained considerable relief of his pain and resumed light work six months after his operation.

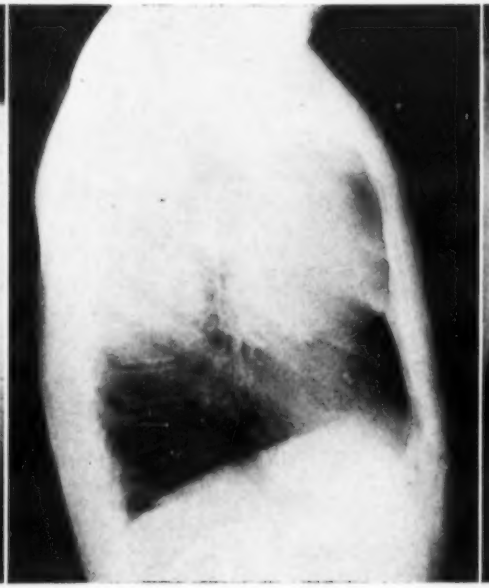
Comments

Relief of the throbbing, pulsating anterior chest pain or the constant dull ache in the back appears to be the most gratifying result of wrapping these intrathoracic aortic aneurysms. Although the original purpose of the procedure was to patch or reinforce weakened artery walls and prevent or delay their rupture, the patients frequently seem more concerned about their immediate symptoms. The one patient who has been examined at autopsy one and one half years after wrapping his aneurysm failed to show any actual shrinking of the aneurysm cavity, although the vessel wall was thickened by a layer of fibrous tissue on both sides of the polythene film. The lack of any decrease in size of the x-ray shadows is to be expected from the pathologic reaction noted in animals in which a thick layer of dense scar tissue is deposited on both sides of the film.

Fusiform aneurysms of the descending aorta offer more favorable opportunities for successful reinforcing with impure polythene than the saccular aneurysms of the ascending aorta and its arch for the following reasons. They are more accessible with less important branches and adjacent vital structures offering a wider surface for covering. They are more apt to produce pain which can be relieved by wrapping. The incidence of cardiac involvement with aortic insufficiency and decompensation appears to be lower in this group.

An obstruction of one of the main bronchi or encroachment on the trachea presents an absolute contraindication to surgery.





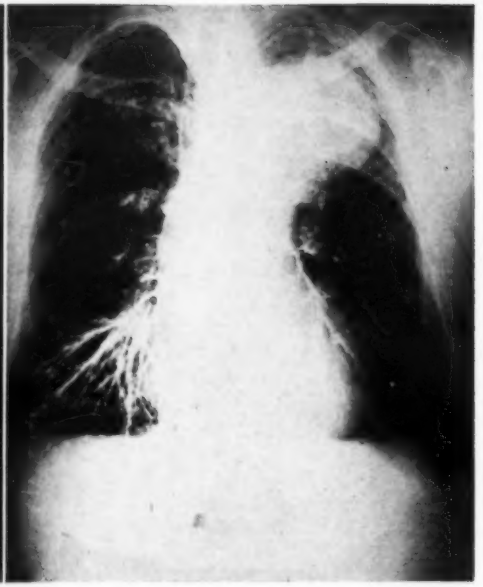


FIGURE 1 FIGURE 2 FIGURE 3

Figure 1 and 2 together: Preoperative chest x-rays of J. E. No. 3, with saccular syphilitic aneurysm of ascending aorta, which was wrapped with polythene film two and one half years ago. This patient is still alive without chest pain although the aneurysm was about to involve the anterior chest wall at the time of operation.—*Figure 3:* Preoperative bronchogram on J. L. No. 7, with saccular syphilitic aneurysm of distal arch of aorta. Bronchogram failed to show obstruction of left main bronchus indicating suitability for surgery.

Severe cardiac decompensation with insufficiency of the aortic valve or erosion of the anterior chest wall both preclude any very satisfactory end result from the procedure even though the patient may withstand the immediate surgery. Arteriosclerotic aneurysms of the abdominal aorta also can be reinforced satisfactorily with impure polythene provided the disease has not already interfered with the circulation of the lower extremities.

CONCLUSIONS

1) Commercial unrefined polythene film has been shown experimentally to produce an extensive fibrous tissue proliferation when placed within the body.

2) This irritative reaction is apparently due to chemical substances added to the pure polythene during its processing.

3) This fibrous tissue reaction of polythene can be employed to reinforce the weakened vessel walls of aneurysms.

4) Nine patients whose intrathoracic aneurysms have been wrapped or patched with polythene are reported.

5) Five of the patients survived for one to three years after surgery with varying degrees of improvement in their symptoms.

6) Four of the patients are still alive, the others having succumbed to their disease.

CONCLUSIONES

1) Se ha demostrado experimentalmente que películas de politena comercial no refinada producen una proliferación extensa del tejido fibroso cuando se las coloca dentro del cuerpo.

2) Aparentemente se debe esta reacción irritante a substancias químicas que se añaden a la politena pura durante su preparación.

3) Se puede utilizar esta reacción fibrosa de la politena sobre los tejidos para fortalecer las paredes debilitadas de aneurismas de vasos sanguíneos.

4) Se informa sobre nueve pacientes cuyos aneurismas intratorácicos han sido envueltos en politena o remendados con esta substancia.

5) Cinco de los pacientes sobrevivieron de uno a tres años después de la operación con varios grados de mejoría de sus síntomas.

6) Cuatro de los pacientes viven todavía, mientras que los otros han muerto de su enfermedad.

REFERENCES

1 Harrison, P. W. and Chandy, J.: "Subclavian Aneuryms Cured by Cellophane Fibrosis," *Ann. Surg.*, 118:478, 1943.

2 Pearse, Herman E.: "Experimental Studies on Gradual Occlusion of Large Arteries," *Ann. Surg.*, 112:923, 1940.

3 Page, I. H.: (a) "Production of Persistent Hypertension by Cellophane," *J.A.M.A.*, 113:2046, 1939. (b) "Method for Producing Persistent Hypertension by Cellophane," *Science*, 89:273, 1939.

4 McKeever, D. C.: "Use of Cellophane as Interposition Membrane in Synovectomy," *J. Bone and Joint Surg.*, 25:576, 1943.
5 Poppe, J. K. and Renault de Oliveira, H.: "Treatment of Syphilitic Aneurysms by Cellophane Wrapping," *J. Thoracic Surg.*, 15:186, 1946.
6 Ingraham, F. C., Alexander, E. Jr. and Matson, D. D.: "Polyethylene," *J.A.M.A.*, 135:82, 1947.
7 Yeager, George H. and Coroley, R. Adams: "Studies on the Use of Polythene as a Fibrous Tissue Stimulant," *Ann. Surg.*, 128:509, 1948.

Discussion

OSLER ABBOTT, M.D., F.C.C.P.
Atlanta, Georgia

It is a great pleasure to discuss Dr. Poppe's paper because I have many pleasant memories of working with him and it was his work that instigated my interest in the subject. I would like to emphasize that I think both our interests were fundamentally aroused in this subject by Dr. Evarts Graham. This work is still in an experimental phase. It has been our policy to consider that experimental surgery must be done essentially on hopeless cases. The individuals on whom we have done this work in Atlanta have, in the main, been patients who came in with the diagnosis of cardiac decompensation or pneumonia in one or both sides. These are the patients Dr. Poppe mentioned as being non-candidates for the operation. They have been our main candidates and we have learned many things from them.

I would particularly like to emphasize the statement of oversoaking in alcohol as we had a sad experience of no reaction at all from the material used after it was soaked too long a time. The boiling method is much better. A few slides will show how we have attacked this problem much of which is purely experimental surgery on the hopeless case. In many cases we have been pleased, in others we have been most displeased, and we feel there is much more to learn about the problem. Certainly in our experience of following up patients who have had partial wrapping of the aneurysms, the results have been quite poor; only 40 per cent of them have had relief of pain and the majority of them that we have had a chance to follow have ruptured the aneurysm within one or two years after the operative procedure. We now make it a routine method, that whenever we wrap an anuerysm incompletely there is concomitant internal wiring of the aneurysm. We have now operated on 32 patients, in whom the aneurysm has been wrapped, and there have been six more in whom decompression has been done, many of whom have felt so well that they have refused further surgery and have thus given us

a comparative series as to what life expectancy is in the decompressed and in the wrapped. Certainly, with decompression there is prelongation of life, but unfortunately the decompression does not last a sufficient length of time to give us a permanent aid; they usually come back with return of symptoms of bronchial compression within about four months after recompression.

JAMES E. DAILEY, M.D., F.C.C.P.
Houston, Texas

We have had the opportunity to wrap three of these aneurysms in the past year, one of the ascending aorta, one of the descending aorta and one of the innominate. The results of course are difficult to evaluate, other than the fact that the patients are relieved of their symptoms of pain and disability and, in our three cases, the patients were completely relieved and are back at work. There was absence of progression of the tumors as seen on the x-ray films. In the case of the aneurysm of the innominate, which could be seen and felt, there was distinct regression in the size of the tumor and absence of visual and tactile pulsations.

With regard to sterilization of the cellophane and the effect that soaking in alcohol has on the substance, we sterilize it by immersion in cyanide solution with apparently good results.

Closing Remarks

J. Karl Poppe, M.D., F.C.C.P.: I should like to congratulate Dr. Abbott on his large series of cases and on his courage in tackling some of these poor risk patients. We know that the more advanced the lesion, the less satisfactory the result. The most favorable results to date in my experience have been with aneurysms of the descending aorta, in which there is less apt to be cardiac complications such as aortic insufficiency and cardiac decompensation. In patients with only pain from involvement of the chest wall and intercostal nerves the possibility of relieving symptoms seems much greater.

A recent communication received from the Dupont Company states that the diecetyl phosphate is slightly soluble in cold alcohol and much more soluble in warm alcohol, suggesting that one might possibly sterilize polythene film in alcohol if kept in the refrigerator; but boiling seems still better.

Nutrition in Far Advanced Tuberculosis
A Preliminary Study*

CYRIL W. ANDERSON, M.D., J. N. MEDEFIND, M.D.,
and J. DWIGHT DAVIS, M.D., F.C.C.P.
Van Nuys, California

This study was initiated to attack the problem of establishing nutritional balance in far advanced pulmonary tuberculous patients and to observe, if possible, whether a proper nutritional balance, in itself, could favorably deflect the downward course of these patients. It was evident that the invariably poor appetites of these patients should be the first point of investigation.

The study of appetite has developed considerable experimental work. There is evidence that the sensation of hunger is directly correlated with increased gastric tone and secretions; this was evident in the fasting experiments of Hoelzel[1] and the x-ray observation of Barclay.[2] Glaessner,[3] in 1943, offered experimental evidence that gastric tone and secretory activity varied inversely with blood sugar volumes. Blotner,[4] in 1945, found that of 70 nondiabetic adults with illnesses causing prolonged physical inactivity, 63 had blood sugar findings indicative of decreased glucose tolerance. There has been evidence that tuberculous patients have a tendency toward decreased glucose tolerance although Kramer's study of 98 tuberculous patients[5] showed only 17 per cent with such a tendency.

In recent years a great deal of importance has been placed upon protein in the diet. This is especially true of the influence of protein on resistance to infection and repair of injured tissues. Cannon[6] in 1943, postulated that a large protein reserve was necessary to maintain proper antibody response and the phagocytic activity of mesenchymal cells. He showed that hypoproteinemic rabbits had markedly lessened ability to produce agglutinins. Madden and Whipple[7] observed in 1940 that blood protein levels directly reflected tissue protein stores. Krebs[8] in 1946, carefully studied the antibody response in a girl with a low total blood protein level and an extremely low gamma globulin fraction. After a full course of immunization with typhoid vaccine, she failed to develop any antibody. The maintenance of high protein levels has

*From the Thoracic Diseases Service, Birmingham Veterans Administration Hospital, Van Nuys, California. Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

been long recognized as necessary to rapid healing of surgical wounds and ulcers. Lund,[9] in 1945, also observed delayed gastric emptying time and edema of surgical stomata in hypoproteinemic patients.

Vitamin studies in relation to tuberculosis have been particularly concerned with vitamins A and C. Goetz, et al,[10] in a study of 275 tuberculous and nontuberculous patients found vitamin A deficiencies particularly in the tuberculous group, increasing in degree with the severity of the tuberculous process. They also noted a marked vitamin C deficiency in the tuberculous group. Sweaney and his associates,[11] in 1941, also noted an unaccountable exhaustion of vitamin C in tuberculous patients, increasing with the severity of the disease. Menkin, et al,[12] in 1934, had demonstrated an apparent action of vitamin C to stimulate fibroblasts to increase connective tissue formation.

To investigate the relationship of appetite to blood sugar levels, we selected 55 patients with far advanced pulmonary tuberculosis. All of these had progressive disease with cavitation and all except four had bilateral involvement. All had shown persistent loss of weight for two to eight months prior to this study. Forty-nine of these patients stated that, although their appetites for breakfast were fairly good, they had little or no appetite for the succeeding two meals which ordinarily are served at four hour intervals.

Six hour glucose tolerance test curves were observed in 47 of these 55 patients. Thirty-seven, or 77 per cent showed definitely abnormal curves and only seven, or 15 per cent had normal tolerance curves. The abnormal curves fell into two distinct types. Twenty-six, or 55 per cent, demonstrated a sharp blood glucose rise in the first half hour with a slow decline, not returning to the base line before three hours; this was designated as a Type I curve. Ten, or 22 per cent, showed a sharp rise continuing beyond the first hour, falling slowly and not returning to the base line until four hours after ingestion of the glucose; this curve was designated Type II. Significantly, all ten patients demonstrating Type II curves were extremely ill; four are now dead and four are terminal. Graphic representation of these glucose tolerance curves are shown in figure one.

On the premise that the poor appetite of these patients might be due to a hyperglycemia prolonged into the next meal period, a two meal diet was devised, composed of an unusually large breakfast and a supper eight hours later, interrupted only by a light noon supplemental feeding. The diet had values of approximately 3400 calories, protein 160 grams, fat 77 grams, carbohydrate 560 grams. Our normal hospital diet has approximately the same caloric value, but definitely lower value for protein.

Although these patients were for the most part on a high vitamin regimen, this experimental diet provided daily supplements of 5000 units A, B and D with 500 mg. of ascorbic acid to obviate the effect of any deficiency factor. Breakfast and supper were approximately the same in nutritional values, with each consisting of from 220 to 250 grams of carbohydrate, 60 grams of protein, and 30 grams of fat. Two hundred and fifty to 400 calories were allotted to a mid-day and an evening supplement consisting of an egg nog formula and cookies. Each patient accepting this diet was provided an intake chart with instructions to chart accurately the proportion of each food item rejected daily. After a short time on the diet it was found that the low fat content decreased the palatability of the diet, which was then changed, raising the fat content to 150 grams at the expense of carborydrate which was reduced to 350 to 370 grams.

Only 24 of the 55 studied as to glucose tolerance would accept the rigid limitations of this diet and keep an intake chart accurately enough to study. These 24 patients recorded on an intake chart the exact proportions of each dietary item taken. Their weight trends for two months prior to the diet and for two months on the diet were tabulated, as well as toxicity evaluations, blood studies, blood protein studies and liver function tests. Nineteen of these patients had marked toxicity evidenced by fever and increased erythrocyte sedimentation rates. Eighteen had compli-

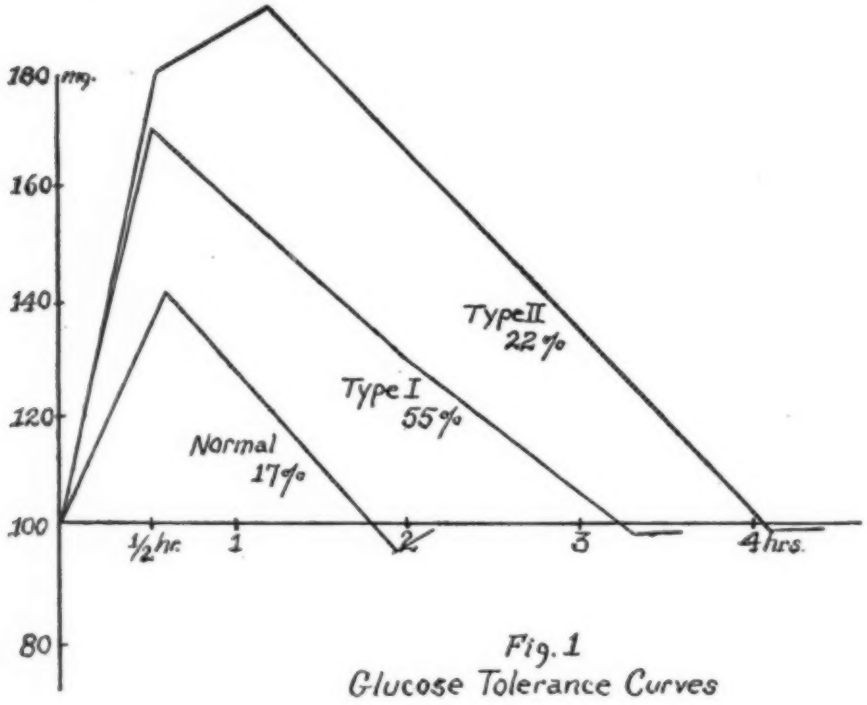


Fig. 1
Glucose Tolerance Curves

cations, including tracheo - bronchial tuberculosis, tuberculous laryngitis, pleural effusion, and genito-urinary tuberculosis. The known duration of their disease was from two to 28 years. These patients, for the most part, were so far advanced and with such extensive disease, that sanatorium care was the only possible immediate therapy. Their normal weight averaged 153 pounds; all had a downward weight trend prior to this study with an average loss per man of 21 pounds.

The 24 patients showed a total net loss of 61 pounds, or 2.5 pounds per man for the two months prior to the diet change. Following two months of the new diet they showed a total net gain of 45 pounds, or 1.9 pounds per man. The distribution of weight changes are shown in Figure two.

We attempted to correlate their intake percentage with weight trends and toxicity, as expressed by fever and increased erythrocyte sedimentation rates. It was found, by studying two week periods, that their weight gain or loss was directly proportional to food intake regardless of fever or general toxic symptoms, and that an intake of 80 per cent was the critical point above which they gained weight and below which they lost. It was noted that of 19 periods studied in patients with an intake of 80 per cent and

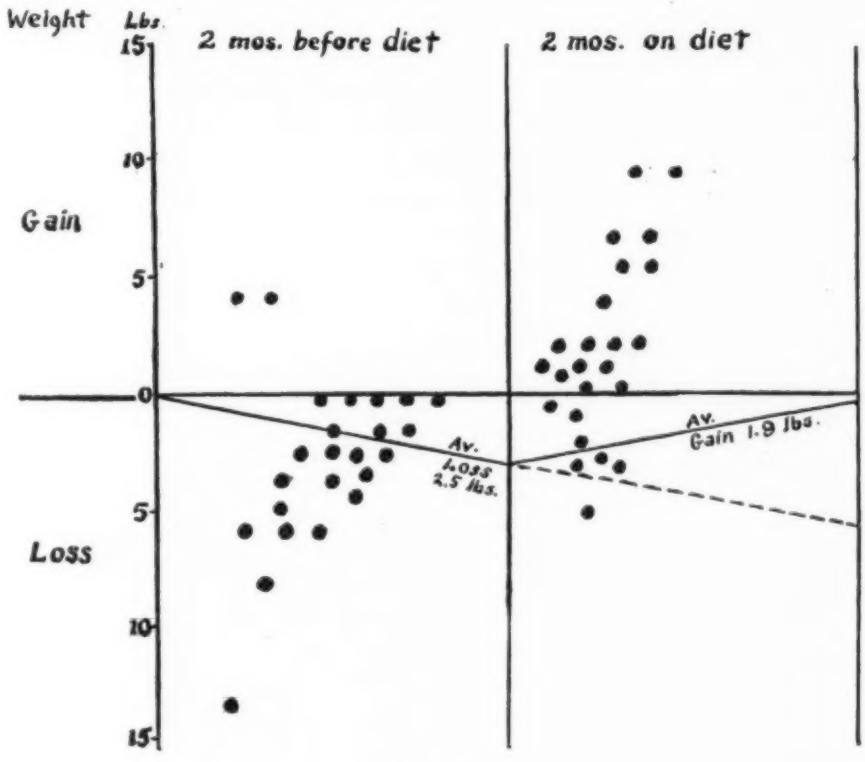


Fig. 2

over, only five showed any loss of weight and of 22 periods studied in patients with an intake of less than 80 per cent, 17 showed loss of weight. At 80 per cent intake, the gains and losses were equal. The elements of food rejected amounted in carbohydrate, protein and fat to approximately the same ratio as in the total diet.

A careful computation and analysis of their intake charts disclosed that these 24 patients had averaged over the two months period on the diet, a daily intake of carbohydrates 297 grams, proteins 119 grams, and fats 120 grams. This natural selection corresponded very closely with 80 per cent of the prescribed diet, i.e., carbohydrates 297 grams, protein 128 grams, fats 120 grams. Since the average weight of these patients was 132 pounds, it might be said that the dietary components necessary to reverse the weight loss trend of this group was, per kilogram of body weight, carbohydrates 5.0 grams, proteins 2.0 grams, fats 2.0 grams. It was also noted that in selecting two week periods during which the patients had fever averaging over 99.6 degrees F, 12 of these with food intake of 80 per cent and over showed weight gain in ten periods and loss in two, one of which was associated with diarrhea. Again, in two febrile periods of two weeks duration with food intake of 80 per cent there was found neither gain nor loss of weight.

Blood protein studies before and after this high protein diet showed no essential change from those of our controls. Total blood proteins remained slightly above the low normal levels. These patients showed generally an increase in globulin and a decrease in albumin fractions, reflecting the general trend of our far advanced tuberculous patients. These fractions approached equality, but never a reversal. We could not determine that our diet influenced this trend. The hemoglobin level showed a general increase with 14 patients showing increase of hemoglobin, five decreased levels, and five maintaining a normal level before and after the diet. Nine patients showing increased hemoglobin levels were in the higher food intake group compared with five in the group with intake of under 80 per cent. Most of the patients expectorated large quantities of sputum. In order to determine if this represented a significant loss of protein, five patients were selected who produced copious amounts of mucopurulent sputa. The largest amount of protein found in any 24 hour accumulation was 1.1 gram.

SUMMARY

1) Decreased glucose tolerance was found in 37 of 47 patients with far advanced pulmonary tuberculosis. These patients all demonstrated poor appetites except for the breakfast meal. The

glucose tolerance curves showed prolongation of hyperglycemic levels beyond the third and fourth hours following ingestion of the glucose. On the premise that their poor appetites for the succeeding meals were due to prolonged hyperglycemia a two meal high protein diet was devised with 8 hours between meals.

2) Careful weight, food intake, and blood protein studies were made on 24 far advanced tuberculous patients on this diet. These patients showed a weight reversal from a previous average loss of 2.5 pounds per man two months prior to the diet to an average gain of 1.9 pounds per man during two months on the diet. A critical level of food intake for weight maintenance in this group was found to be 2700 calories divided into 297 grams carbohydrates, 128 grams protein and 120 grams fat. Above this level the great majority of these patients gained weight regardless of fever or other evidence of toxicity.

3) Hemoglobin levels of patients on this diet showed a general increase over the levels 2 months prior to the diet. Total blood proteins showed no essential change over those of the controls. Protein loss in the sputum was found to be negligible.

RESUMEN

1) En 37 de 47 pacientes con tuberculosis pulmonar avanzada se encontró disminución de la tolerancia a la glucosa. Todos estos pacientes tenían mal apetito excepto en el desayuno. Las curvas de la tolerancia a la glucosa revelaron prolongación de los niveles hiperglicémicos por más de tres o cuatro horas después de la ingestión de la glucosa. Sentando como premisa que sus malos apetitos en las comidas subsiguientes se debían a la prolongada hiperglicemia, se ideó una dieta alta en proteínas que consistió de dos comidas separadas por ocho horas.

2) Se llevaron a cabo estudios cuidadosos del peso, la ingestión de los alimentos y las proteínas de la sangre en 24 tuberculosos muy avanzados sometidos a esta dieta. Estos pacientes revelaron una reversión del peso de un promedio anterior de pérdida de 2.5 libras por hombre, dos meses antes de comenzar la dieta, a un promedio de aumento de 1.9 libras por hombre durante los dos meses de dieta. Se encontró que el nivel crítico de ingestión de alimentos necesario para mantener el peso en este grupo fue de 2,700 calorías, divididas en 297 gramos de carbohidratos, 128 gramos de proteínas y 120 gramos de grasas. Con dietas más altas de este nivel la gran mayoría de esos pacientes ganaron en peso, a pesar de fiebre u otros signos de toxicidad.

3) Aumentaron los niveles de la hemoglobina en los pacientes en esta dieta, comparados con los niveles de dos meses antes de la dieta. El total de las proteínas de la sangre, comparado con el

de los testigos, no mostró alteración significativa. Se encontró que fue menospreciable la pérdida de proteína en el esputo.

REFERENCES

1 Hoelzel, R.: "Explanation of Appetite," *Am. J. Digest, Dis.*, 11:71, 1944.
2 Barclay, A. E.: "Mechanics of Digestive Tract," *Lancet*, 1:11, 1934.
Barclay, A. E.: "Normal Stomach," *Lancet*, 2:261, 1922.
3 Glaessner, C. L.: "Gastric Secretion and Sugar Metabolism," *Am. J. Digest, Dis.*, 10:307, 1943.
4 Blottner, H.: "Effect of Prolonged Physical Inactivity on Tolerance of Sugar," *Arch. Int. Med.*, 75:39, 1945.
5 Kramer, D. W.: "Glucose Tolerance in Pulmonary Tuberculosis," *J. Lab. and Clin. Med.*, 18:1212, 1933.
6 Cannon, P. R., Chase, W. E. and Wissler, R. W.: "Relation of Protein Reserve to Antibody-production; Effects of Low Protein Diet and of Plasmapheresis upon Formation of Agglutinins," *J. Immunol.*, 47: 133, 1943.
Cannon, P. R.: "Antibodies and Protein-Reserves," *J. Immunol.*, 44: 107, 1942.
7 Madden, S. C., Finch, C. A., Swasbach, W. G. and Whipple, G. H.: "Blood Plasma Protein; Production and Utilization," *J. Exper. Med.*, 71:283, 1940.
8 Krebs, E. G.: "Depression of Gamma Globulin in Hypoproteinemia Due to Malnutrition," *J. Lab. and Clin. Med.*, 31:85, 1946.
9 Lund, C. C. and Levenson, S. M.: "Protein in Surgery," *J.A.M.A.*, 128: 95, 1945.
10 Getz, H. R. and Koerner, T. A.: "Vitamin Nutrition in Tuberculosis," *Am. Rev. Tuberc.*, 47:274, 1943.
11 Sweaney, H. C., Clancy, C. L., Radford, M. H. and Hunter, V.: "Body Economy of Vitamin C in Health and Disease, with Special Studies in Tuberculosis," *J.A.M.A.*, 116:469, 1941.
12 Menkin, V., Walbach, S. B. and Menkin, M. F.: "Formation of Intercellular Substances by Administration of Ascorbic Acid," *Am. J. Path.*, 10:569, 1934.

Cervical Vagus—Sympathetic Block in Pulmonary Embolism*

WILLIAM A. WERNER, M.D. and
LEWIS H. FERGUSON, JR., M.D.
St. Louis, Missouri

The consequences of pulmonary embolism are at best poorly understood. It has long been evident that factors other than the mere interruption of a vessel supplying a lung segment are operating to produce the clinical picture of pulmonary embolism.

Varying importance has been attached to the sudden strain embolism may impose on the right side of the heart. The degree of mechanical obstruction in the pulmonary circulation is certainly a major element in some cases. This mechanical stress is modified by reflexes arising in the pulmonary vascular bed, although the presence of a pulmono-coronary reflex is difficult to prove.

James Currens[1] states that any actual coronary insufficiency is best explained by shock and a rise in the pressure in the right heart chambers. The venous drainage and Thesbian vessels empty mainly into the right side and are impeded by increased right heart pressure. If the cardiac function should be compromised by pre-existing disease, a sizeable pulmonary obstruction, or relative coronary insufficiency, the development of an acute cor pulmonale would easily explain the picture.

However, often the symptoms of shock and collapse may predominate even with small emboli,[2] when neither electrocardiogram nor postmortem examination reveals evidence of cor pulmonale. A major role of reflex vaso and bronchospasm is postulated in such instances of embolism, but this role is difficult to evaluate at this time. The work of Boyer and Curry[3] indicates that in dogs pulmonary embolism causes reflex bronchoconstriction of a transient nature and some doubt is cast upon its practical importance. Their observations also suggest that reflex bronchospasm may be dependent on a pressure rise in the pulmonary artery and the right side of the heart. Megebow, Katz, and Feinstein[4] gathered evidence to show that the acceleration in respiration was also due to this pressure increase.

deTakats, Fenn, and Jenkinson[5] cite evidence to show that reflex bronchospasm with increased bronchial secretion occurs in the

*From St. John's Hospital, St. Louis, Missouri.

experimental animal. They believe that these two factors produce an atelectasis which accounts for the radiologic picture of infarction and perhaps many of the symptoms of embolism.

Whatever the eventual role assigned to each of these elements, it remains that our present rationale of therapy is directed at relief of the reflex spasms as well as supporting the circulation and the respiratory center. Oxygen, papaverine, and ephedrine seem to have met these requirements reasonably well.

Villaret, Justin-Besancon, and Bardin,[6] investigating pulmonary embolism, found that vagotomy along with ephedrine and atropine all acted favorably in increasing dog's tolerance to repeated emboli and in delaying embolic death. The opposite effect was obtained by section of the cervical sympathetic nerves. The reflex inhibition of the sympathetic system was responsible for hastening sudden death, but there may also be other factors acting, since the rate of discharge from the respiratory center is slowed to a less extent in animals with pulmonary embolism than in normal animals. Thus deterioration may be postponed by the lessened oxygen requirements of the center. Also, the purity of the sympathetic and vagus trunks has become ever less impressive. Katz,[7] for example, now has evidence that the vagi are coronary dilators, not constrictors, and the sympathetic nerves cause both a vasodilitation and vasoconstriction of the coronaries when the effect on cardiac work and metabolism is not considered.

Elimination of both vagal and sympathetic influence was attempted by Skvortsov[8] in a variety of war casualties such as open pneumothorax and lesions of the upper extremities. A vagus-sympathetic block in the neck was performed with procaine infiltration on men who were in a state of shock. In the cases of open pneumothorax, pain and dyspnea disappeared in about 91 per cent, the cough reflex disappeared, and the manifestations of shock gradually vanished in the course of one to two hours. A similar procedure was carried out in the following instance:

CASE REPORT

Mrs. E.L.H., a 41 year old housewife, entered the hospital October 25, 1947 complaining of pain in abdomen with nausea and vomiting for about seven weeks. Physical examination revealed marked tenderness over the right upper quadrant. Her daily temperature reached 103 degrees. RBC, 2.9; Hb, 8.5; WBC, 8650. Attempts to visualize the gall bladder radiologically were unsuccessful. The patient did not respond to chemotherapy. A diagnosis of ruptured gall bladder with abscess formation was made. She was prepared for surgery and operated on November 10, 1947.

She was found to have a ruptured gastric ulcer with a grapefruit sized abscess inferior to the gall bladder. Her postoperative course remained febrile and on December 5, 1947 she developed phlebitis of the right leg.

In view of a prothrombin time of 50 per cent of normal and suspected liver disease, anticoagulant therapy was withheld.

Upper abdominal pain with fever continued and on December 17, 1947 a subdiaphragmatic abscess was drained. On January 3, 1948 she began complaining of frontal headache which seemed to improve somewhat after several days. On January 21, 1948 she experienced sudden left upper quadrant pain with a large tender spleen and a diagnosis of splenic infarct was made. Five days later visual impairment, a choked optic disk on the right, and left sided weakness appeared and a diagnosis of brain abscess was made.

On the following day at 1:00 p. m. the patient suddenly experienced a severe pain in her right lower chest. She became increasingly dyspneic and cyanotic and lapsed into coma and severe shock. Nasal oxygen was begun. She was given morphine gr. 1/6 and papaverine gr. 1 intravenously and subcutaneously.

The patient continued downhill and after one-half hour her respirations were slow and gasping and her cyanosis was extreme. At that time a three inch needle was inserted just behind the posterior border of the sternomastoid at midpoint. The needle was advanced medially and anteriorly about 1½ inches and 10 cc. of 1 per cent novocain was slowly injected, directing the needle superiorly and inferiorly.

Within two to three hours the patient had emerged from shock and her respirations were approaching normal. A short time thereafter she was again conscious. She died several days later of multiple liver and brain abscesses.

It is realized that an accurate estimate of the role of each of the measures employed cannot be made. It may be maintained that this woman might have survived her pulmonary embolus without the vagus-sympathetic block. We can only say that in the opinion of those who saw her it is highly unlikely. The rapidity with which this patient emerged from profound shock and established fairly normal respiration was remarkable. This is a relatively simple and inoccuous procedure and deserves a more thorough trial in cases of shock resulting from pulmonary embolism, and even, perhaps, in shock arising from insult to any abdominal or thoracic viscera, including the heart.

SUMMARY

In the production of the clinical picture of pulmonary embolism, varying importance has been attached to pressure changes in the pulmonary circulation, reflex vaso- and bronchospasm, and reflex production of pulmonary atelectasis. Atropin and vagatomy aid to increase tolerance to pulmonary emboli in dogs. Skvortsov used with success a cervical vagus-sympathetic block with procaine in a variety of war casualties in which shock complicated wounds of the chest and upper extremities. A case of pulmonary embolism followed by severe shock is presented in which cervical vagus-sympathetic block was used successfully.

RESUMEN

En la producción del cuadro clínico de la embolia pulmonar, se les ha atribuído variable importancia a las alteraciones de la presión de la circulación pulmonar, al vasoespasmo y broncoespasmo reflejos y a la producción refleja de la atelectasia pulmonar. En los perros, la atropina y la vagotomía ayudan a aumentar la tolerancia a la embolia pulmonar. Skvortsov empleó con buen éxito un bloqueo vago-simpático cervical con procaína en una variedad de heridos de guerra en los que el choque complicaba a heridas del tórax y de las extremidades superiores. Se presenta un caso de embolia pulmonar seguida de choque grave en el que se empleó con buen éxito el bloqueo vago-simpático cervical.

REFERENCES

1 Currens, James: "The Electrocardiogram in Pulmonary Embolism," *Pros. Staff Meet., Mayo Clinic,* 17:502, 1942.

2 Murnaghan, D., McGinn, S. and White, P. D.: "Pulmonary Embolism with and without Acute Cor Pulmonale, with Especial Reference to the Electrocardiogram," *Amer. Heart J.,* 25:573, 1943.

3 Boyer, Norman H. and Curry, John J.: "Bronchospasm Associated with Pulmonary Embolism, Respiratory Failure," *Arch. Int. Med.,* 73:403, 1944.

4 Megebow, N. S., Katz, L. N. and Feinstein, M.: "Kenetics of Respiration in Experimental Pulmonary Embolism," *Arch. Int. Med.,* 71:536, 1943.

5 de Takats, Geza, Fenn, G. K. and Jenkinson, E. L.: "Reflex Pulmonary Atelectasis, *J.A.M.A.,* 120:686, 1942.

6 Villaret, M., Justin-Besancon, L. and Bardin, P.: "Physio-Pathologie des Accidents Mortels Consecutifs aux Pulmonaires," *Bull. et mem. Soc. med. d. hop. de Paris,* 52:936. "Recherches sur Prevention Experimentales des Accidents Consecutifs aux Embolies Pulmonaires," *ibid,* 52: 941, 1936.

7 Katz, L. N.: "A Survey of Recent Developments Concerning the Concepts of Coronary Disease and Its Management," *Ann. Int. Med.,* 27: 705, 1947.

8 Skvortsov, S. P.: "Cervical Vagus-Sympathetic Block in the Treatment of Shock," *Khirurgiya,* Moscow, 4:3, 1944.

EDITORIAL

DISCRETION IN THE USE OF BRONCHOGRAPHY

To the pilot of preradar days, "visibility unlimited" meant most things in flying. Even the finest pilot needed it. To physicians and surgeons confronted with disease of the lungs, the visibility afforded by radiolucency is the factor that means accuracy of diagnosis and of effective therapy. The use of contrast media increases visibility and extends diagnostic accuracy of x-ray examinations when properly used. Bronchography can be used to outline the ramifications of the bronchial system and demonstrate bronchiectasis and occasionally bronchial stenosis and obstruction. If the oil could be entirely and completely eliminated after bronchography such aid as it gives would be unadulterated with disadvantage.

After bronchography, iodized oil is not completely eliminated for at least two weeks on the average and, while in the lung, it is relatively dense to x-rays and incites an inflammatory reaction. The densities created tend to obscure underlying pathologic change. The pneumonitis diminishes respiratory reserve and produces a palpable nodularity and induration of the lung. There are occasions when these factors are of real significance. If there is a disease process within the lung which is subject to change, such as tuberculosis, abscess, or pneumonitis, it is important not to confuse the picture unnecessarily by superimposing additional densities. If there is marked dyspnea or a low respiratory capacity from any cause, the added burden of an oil pneumonitis may result in pulmonary insufficiency. When surgical treatment is or may be urgent, as in bronchogenic carcinoma, any added limitation of respiratory function greatly increases the risk. Delay of such surgery is equally serious. If thoracotomy is necessary, the nodularity and induration of the pneumonitis so produced make determination of the extent of the primary disease process difficult and introduce a serious factor of error.

Recently, a 59-year-old dentist was admitted with a nine-month history of "virus pneumonia," progressive cough, and severe dyspnea. Shortly before admission, he had had a roentgen-ray examination which revealed a density in the right lung and an extreme degree of mediastinal shift to the right. There was a slight suspicion of lymphangitic spread to the contralateral lung. Apparently for the purpose of demonstrating the suspected bronchial obstruction, a bronchography had been performed immediately. This demonstrated a block in the right mainstem bronchus, but a considerable amount of the oil entered the left lung and subsequently the patient became orthopneic and cyanotic and, although slightly improved at the time of admission seven days later, he was dyspneic sitting up in bed and his fingertips and lips were cyanotic. There was mediastinal shift to the right with dullness and absent breath sounds and scattered, moist rales throughout the left lung. He was unable to hold his breath for more than ten seconds. Bronchoscopy demonstrated a sharp, mobile carina and a fungating tumor extending to within one centimeter of the carina on the medial wall of the right mainstem bronchus. The biopsy was reported as Epidermoid Carcinoma, Grade II. X-rays were taken in an attempt to determine the question of lymphangitic spread to the contralateral lung, but the residual oil and the associated pneumonitis effectively obscured any evidence thereof. Pneumonectomy was delayed for six days at which time his dyspnea had moderated and he was able to hold his breath for sixteen seconds. Bronchography in this particular case served no useful function and failed to establish either a positive diagnosis or the possibility of resectability. It may have obscured evidence of spread to the left lung and it definitely did aggravate the dyspnea to a serious degree and delay urgent surgery.

With the increasing use of lipiodol by physicians and radiologists in the diagnosis of pulmonary disease, there has been a certain lack of discrimination in its use which the preceeding case illustrates. Contrast media must not be used in the lung fields unless it can be said that (1) its use will not obscure important changes in the pulmonary parenchyma, (2) it will not seriously aggravate a pulmonary insufficiency, and (3) it will not prove a complicating factor in therapy.

Richard H. Overholt, M.D., F.C.C.P. and Beatty H. Ramsey, M.D.,
Boston, Massachusetts.

Fifteenth Annual Meeting

AMERICAN COLLEGE OF CHEST PHYSICIANS

As this issue of the journal goes to press the *Fifteenth Annual Meeting* of the College will be in session at the Ambassador Hotel, Atlantic City. Advance reservations indicate that there will be a record attendance at this meeting. Subscriptions for the Round Table Luncheon Meetings have been received at the Executive Offices in such numbers as to assure a capacity attendance at each of the luncheons. Arrangements have been made for meetings of the Board of Regents, Board of Governors, Executive Council, and all other councils and committees of the College.

A very interesting scientific program has been arranged by the Committee on Scientific Program and papers on a great variety of subjects will be presented by outstanding authorities in their fields. New features in the program will include critical reviews in chemotherapy, respiratory physiology, roentgenology, medical aspects of diseases of the chest and thoracic surgery, and a motion picture session devoted to diseases of the chest. One afternoon session will be devoted to an x-ray conference. Reports of the meeting will be published in future issues of *Diseases of the Chest.*

College Chapter News

FLORIDA CHAPTER

At the first meeting of the Florida Chapter, held in Belleair on April 10, the following officers were elected for the chapter:

E. C. Brunner, M.D., Miami, President
Arnold S. Anderson, M.D., St. Petersburg, Vice-President
Howard K. Edwards, M.D., Miami, Secretary-Treasurer.

NEW ENGLAND STATES CHAPTER

The New England States Chapter held its annual meeting at the Deaconess Hospital, Boston, Massachusetts, on May 11. Dr. Walter L. Phillips of Capetown, South Africa was the guest speaker; he spoke on "Tuberculosis Problems in South Africa" and also presented a very interesting film in which a hydatid cyst of the lung was treated by means of a lobectomy. The newly elected officers of the chapter are:

Moses J. Stone, M.D., Boston, Massachusetts, President
Hubert A. Boyle, M.D., New Bedford, Massachusetts, Vice-President
John B. Andosca, M.D., Mattapan, Massachusetts, Secy.-Treas.

NEW JERSEY CHAPTER

At the annual meeting of the New Jersey Chapter held in Atlantic City on April 28, the following officers were elected for the ensuing year:

Homer H. Cherry, M.D., Paterson, President
Joseph A. Smith, M.D., Glen Gardner, First Vice-President
Juan R. Herradora, M.D., Jersey City, Second Vice-President
Benjamin P. Potter, M.D., Jersey City, Secretary-Treasurer.

NEW YORK STATE CHAPTER

At the annual meeting of the New York State Chapter of the College, held in Buffalo on May 5, the following officers were elected:

Roger A. Hemphill, M.D., Mt. Morris, President
Joseph J. Witt, M.D., Utica, First Vice-President
David Ulmar, M.D., New York, Second Vice-President
Donald R. McKay, M.D., Buffalo, Secretary-Treasurer.

OHIO CHAPTER

The Ohio Chapter held its annual meeting at the Neil House, Columbus, on April 20, at which time the following officers were elected for the ensuing year:

Karl P. Klassen, M.D., Columbus, President
Lynne E. Baker, M.D., Dayton, Vice-President
E. F. Conlogue, M.D., Dayton, Secretary-Treasurer.

POTOMAC CHAPTER

At the annual meeting of the Potomac Chapter, held in Baltimore on April 27, the following officers were elected for the year 1949-1950:

Edgar W. Davis, M.D., Washington, D. C., President
Hugh G. Whitehead, M.D., Baltimore, Maryland, Vice-President
Milton B. Kress, M.D., Towson, Maryland, Secretary-Treasurer.

ROCKY MOUNTAIN CHAPTER

Dr. Ralph G. Rigby, Salt Lake City, Utah, President of the Rocky Mountain Chapter, has announced the following committee appointments:

Program Committee:

H. M. Van der Schouw, M.D., Wheatridge, Colorado, Chairman
John B. Grow, M.D., Denver, Colorado
Carl W. Tempel, M.D., Denver, Colorado
W. R. Rumel, M.D., Salt Lake City, Utah.

Publicity Committee:

John S. Bouslog, M.D., Denver, Colorado, Chairman
Fred Harper, M.D., Denver, Colorado
Carl H. Gellenthien, M.D., Valmora, New Mexico
Robert C. Cook, M.D., Ft. Logan, Colorado

General Arrangements Committee:

Arnold Minnig, M.D., Denver, Colorado, Chairman
B. T. McMahon, M.D., Denver, Colorado
Lorenz W. Frank, M.D., Denver, Colorado
James H. Forsee, M.D., Denver, Colorado.

TEXAS CHAPTER

The following officers were elected at the annual meeting of the Texas Chapter held in Houston on May 2nd:

Jesse B. White, M.D., Amarillo, President
David McCullough, M.D., Kerrville, First Vice-President
Charles J. Koerth, M.D., San Antonio, Second Vice-President
Henry R. Hoskins, M.D., San Antonio, Secretary-Treasurer.

CALIFORNIA CHAPTER

At the annual meeting of the California Chapter of the College held in Los Angeles on May 8, the following officers were elected for the coming year:

Lyman A. Brewer, M.D., Los Angeles, President
Seymour M. Farber, M.D., San Francisco, Vice-President
C. Gerald Scarborough, M.D., San Jose, Secretary-Treasurer.

ANNUAL REPORT, SOUTH AFRICAN CHAPTER

The first Chapter of the American College of Chest Physicians in the Union of South Africa was organized on April 28, 1948. There are 25 members of the College in the Union of South Africa, with David P. Marais, M.D., as Regent. The 16 members residing in the Southern States have formed the above Chapter with Theodore Schrire, M.D., as Governor, and when a sufficient number of members of the College are enrolled in the Northern States, it is planned to charter a chapter for that district. P. J. Kloppers, M.D., is Governor for the Northern States.

The early meetings of the Chapter were largely taken up by detailed discussions of the aims and objectives of the Chapter and it was the general opinion that the group should become interested in the problem of tuberculosis in South Africa, as well as to conduct scientific programs in chest diseases. At one of the meetings, the various aspects of pleural effusion were discussed in a series of papers and a paper was also read on atelectasis. One evening was devoted to the showing of films and other meetings were occupied by the presentation of brief clinical cases and records presented by members of the College.

All of the meetings were well attended and the enthusiasm of the Fellows was equalled only by the high order of the scientific discussions.

s/ H. H. Jacob, M.D., F.C.C.P., Secretary-Treasurer.

CUBAN CHAPTER

On April 26th, at the Academy of Sciences, Havana, Cuba, the Cuban Chapter of the College presented a Round Table Conference on Pulmonary Abscess. Antonio Navarrete, M.D., Regent of the College, presided at the meeting and reported a large attendance. Francisco J. Menendez, M.D., President of the Cuban Chapter of the College was one of the speakers. Other speakers were Francisco Perez Carballas, M.D., Pedro L. Fariñas, M.D., Rufino Moreno, M.D., Orfilio Suarez de Bustamente, M.D., and Rogelio Barata, M.D.

PORTUGUESE CHAPTER ORGANIZED MARCH 27, 1949

On March 27, 1949, the organizational meeting of the Portuguese Chapter of the American College of Chest Physicians took place in Coimbra, Portugal. The following officers were elected:

Augusto Vas Serra, M.D., Coimbra, President
Antonio S. Araujo, M.D., Porto, Vice-President
Lopo Cancella, M.D., Lisbon, Secretary-Treasurer.

Lopo de Carvalho, M.D., Governor of the College for Portugal stated that Coimbra was selected as the sight for the first meeting in homage to the University of Coimbra, where the first school of medicine was established.

College News Notes

Dr. E. W. Hayes, Monrovia, California, Past-President of the College, has been elected President of the California Tuberculosis and Health Association to succeed Dr. Harry C. Warren, San Francisco, Second Vice-President of the College.

Dr. Carl C. Aven, Atlanta, Georgia, has been appointed Chairman of the Board of Governors of the College to complete the unexpired term of Dr. Robert K. Campbell of Springfield, Illinois, who has resigned the office because of illness. Dr. Italo Volini, Chicago, Illinois, has been appointed to serve the unexpired term of Dr. Campbell as Governor of the College for Illinois.

Dr. William C. Voorsanger, San Francisco, California, received the annual award of the California Tuberculosis and Health Association for meritorious service in the field of tuberculosis control. The presentation was made by Dr. R. S. Sundberg of San Diego, California.

Dr. Chevalier L. Jackson, Philadelphia, Pennsylvania, has recently returned from Mexico City where he participated in a postgraduate course in bronchoesophagology.

Dr. Leon Unger, Chicago, Illinois, is leaving for a visit to Great Britain early this month.

The Council of Tuberculosis Hospitals of the College held a meeting at the Congress Hotel, Chicago, on April 9th. The following members of the council attended the meeting: Dr. R. S. Anderson, Erie, Pennsylvania, Chairman; Dr. E. W. Custer, South Bend, Indiana; Dr. Charles A. Brasher, Mount Vernon, Missouri; Dr. E. F. Conlogue, Dayton, Ohio, and Dr. David F. Loewen, Decatur, Illinois. The council will make a report of its activities at the annual meeting of the College.

Dr. Otto L. Bettag has been appointed as medical superintendent and tuberculosis control officer of the Municipal Tuberculosis Sanitarium, Chicago, Illinois. Dr. Bettag was formerly medical director of the Livingston County Tuberculosis Sanatorium in Pontiac, Illinois.

Book Reviews

THE CHEST AND THE HEART, By J. Arthur Myers and C. A. McKinlay. Charles C. Thomas, Publisher, Springfield, Illinois.

J. Arthur Myers did it again. With the assistance of C. A. McKinlay he has compiled in two volumes 1800 pages of pertinent information on diseases of the chest. Undoubtedly realizing the importance of heart problems in diseases of the chest, Dr. Myers mobilized such cardiologists as Willius, George Herrmann, Ralph Major and a number of other equally well known men to contribute on the heart. It makes one feel happy to realize that chest specialists do not any longer concern themselves only with tuberculosis of the lungs.

Myers and McKinlay compiled this two volume edition with the aid of sixty-one experienced specialists. Scammon, Rasmussen, and Myers wrote respectively on the embryology, innervation and gross anatomy of the chest. Maurice Visscher and Victor Lorber devoted thirty interesting pages to the physiology of respiration.

Among the numerous topics discussed by Dr. Myers himself, one may read on the diseases of the diaphragm, diseases of the mediastinum, diseases of the trachea, and bronchi, pulmonary abscess, syphilis, glanders and anthrax, pulmonary emphysema, inhalation of fumes, gases, and vapors, inhalation of dusts, air-borne infections, air conditioning, the tubercle bacillus, first infection type of tuberculosis, reinfection type of tuberculosis, treatment by intrapleural artificial pneumothorax, tuberculosis of the lymphatic system, tuberculosis case finding and finally veterinarian's contribution to control of tuberculosis.

C. A. Stewart wrote on the normal chest in infancy and childhood. Porter Vinson discussed diseases of the esophagus. Kinsella took up chest injuries, while Simons and Stuart Harrington discussed respectively malignancies of the chest, and benign intrathoracic tumors.

Harold S. Diehl devotes 18 pages to an excellent discussion of all important phases of the common cold. Hinshaw wrote two chapters on pulmonary edema and pulmonary embolism. Adamson discussed pulmonary atelectasis, while Moorman took up cystic diseases of the lungs.

Surgical features have been written up by Thomas J. Kinsella and Richard Davison.

Chapters on mycoses of the lungs were contributed by Henrici and Emmons, Towey, David T. Smith, and Farness. The chemistry of the tubercle bacillus was discussed by Long and Seibert. The chapters on artificial pneumoperitoneum and tuberculosis of the abdomen were written by Edward H. Hayes. Mc Kelvey wrote two chapters on gynecological tuberculosis and tuberculosis in obstetrics. Bone and joint tuberculosis was covered by John H. Moe. Tuberculosis of the nervous system is written up by John E. Skogland. Francis M. Walsh covered tuberculosis of the eye, and Michelson and Layman discussed tuberculosis of the skin. Erythema nodosum was taken up by Wesley W. Spink. Epidemiologic phases of tuberculosis were covered in three chapters by Hilleboe and also Myers.

The second section of the "Chest and the Heart" takes up about 400 pages jam packed with information about the heart.

Part one takes up in one chapter the examination of the normal heart and blood vessels and in another chapter normal heart beat and the carotid sinus reflex, both chapters ably written by S. Marx White. The

chapter on venous pressure and circulation time is discussed by George N. Aagaard. The roentgenology of the heart is taken up by Ungerleider and Gubner. The physiologic and physical aspects of the electrocardiogram are discussed by Richard Ashman.

Part two takes up congenital heart disease, cor pulmonale and diseases of the great vessels. Sako writes on congenital heart disease, Willius discusses cor pulmonale, and Tuohy takes up the great vessels.

Part three includes the heart in pregnancy, discussed by Jensen; cardio-vascular disturbances written by George Herrmann. The chapter on cardiac arrhythmia is contributed by Peter Bohan, while the chapter on the heart in thyroid disease is considered by C. A. McKinlay.

Four chapters are devoted in part four to infectious heart disease. Hansen writes the chapter on rheumatic heart disease. The chapters on pericarditis and valvular disease are taken up by Willius, while Ralph Major considers endocarditis in another chapter.

Part five contains three chapters on hypertension and degenerative heart disease. The chapter on hypertension is written by Page, while Nadler discusses hypertensive heart disease, and Barnes takes up coronary sclerosis.

Part six takes up the prevention and treatment of heart disease in three chapters. Glomset discusses the prevention of premature heart failure. Hirschboeck writes on the treatment of heart failure, and Richard Davison takes up cardiac surgery.

In an appendix of twenty pages Harry C. Sweany ably discusses the pathogenesis of tuberculosis.

The "chest and the heart" written and compiled by Myers and McKinlay with over sixty competent authors contributing on all phases of diseases of the chest which naturally includes the heart, the mediastinum, the chest wall and the diaphragm brings together in two volumes encyclopedic information regarding any and most all phases of diseases of the chest. The literature on the various topics is brought down to 1946 and in many cases to 1947. The method of approach is both purely scientific and also practical from the view point of clinical application. The illustrations and charts are very illuminating. The combined author and subject index to which about 60 pages are devoted, makes "the chest and the heart" an indispensable reference book on diseases of the chest.

This book is an anthology of the most recent information on problems involving the chest organs. It is truly a ready reference book well adapted for the medical student, the general practitioner, as well as the specialist on diseases of the chest.

M. Joannides, M.D.

TUBERCULOSIS (A Discussion of Phthisiogenesis, Immunology, Pathologic Physiology, Diagnosis, and Treatment), by Francis Marion Pottenger, A.M., M.D., LL.D., F.A.C.P., Emeritus Professor of Medicine, University of Southern California, the School of Medicine; Medical Director, the Pottenger Sanatorium and Clinic for Diseases of the Chest, Monrovia, California. Published by The C. V. Mosby Company, St. Louis, Missouri, 1948.

Rarely does it fall to the lot of one man to bridge completely two generations of medicine. Dr. Pottenger is one of those men. Although many changes have taken place in the handling of tuberculosis since the first two volume set on Pulmonary Tuberculosis was published, he

has adapted himself exceedingly well to the changes and has made a valuable contribution in the present volume.

The author's own apology for devoting so much space to phthisiogenesis seems to this reviewer, unwarranted. The discussion is scholarly, accurate and pertinent. In the classical clinical fields the work is unsurpassed. The writing is clear; it is easy and actually pleasant to read; the text is concise, complete and generally correct—just what one would expect from a man of Dr. Pottenger's vast experience.

It would be expecting too much—in fact the impossible—however, to hope for one man to have everything perfect under the circumstances. Every one has his special interests that may be over-played and other useful ideas not sufficiently emphasized. In a minor degree, this text is no exception. For example, in a modrate sized text, it would seem that a little too much emphasis is placed on the problems of reflexes. There are probably few clinicians today who make use of anything but the elementary aspects of the "spasm" and "atrophy" of muscles overlying the diseased lung. Since most books are predominantly utilitarian, there would seem to be much academic discourse that could well have been left to larger treatises. Not that the discussion isn't interesting, scientific and even profound, but there are so many interfering factors arising within the chest, that the use of the reflex signs are limited, more than the text would lead one to believe.

The same points may be raised to the use of tuberculin in treatment. Tuberculin was used in treatment at the turn of the century and can still be used effectively by Dr. Pottenger and a few others in certain types of disease. But the same may be said of gold treatment, yet few texts mention the latter and the former should probably merely be mentioned today in passing. The temptation is great for a man with such a storehouse of knowledge to refrain from dilating on a method that he knows so well and knows how to use so well. Yet nothing can contradict the fact that the use of tuberculin in treatment of tuberculosis is passé and, that after all, the book is limited in space.

The "dilution-flotation" method of finding tubercle bacilli is another "favorite" that is mentioned to the exclusion of all other methods. Not that the method isn't good. It is. But most workers have found the method too time consuming for ordinary use and if a more laborious method *must* be used, bronchial aspiration surpasses all others, especially when the aspired material is cultured. The common methods should have been mentioned such as those advocated by the American Trudeau Society. This reviewer does not subscribe to the statement "that every student is familiar" with the "usual method of examining sputums." Under no circumstances is the finding of tubercle bacilli in either the early, the complicated, or the healing case, a matter for "students." Especially is that true with the culture method of diagnosis which the author has failed to mention.

The chapter on the x-ray could have recommended the use of lateral, oblique, lordotic positions as well as planographs and "spot" pictures. In the complications of the disease, genito-urinary, bone, joint, adrenal, miliary, meningeal, cold abscesses and other disease localizations might have been mentioned to advantage. The subjects the author does discuss, such as hemorrhage, enteritis, pleurisy, etc., however, are classics. The chapter on compression therapy only gives one small paragraph to pneumoperitoneum and none at all to extrapleural pneumothorax

and segmental resection. While extrapleural pneumothorax is unquestionably controversial, yet there are a sufficient number of advocates of the method to warrant mention. On Page 557, Figure 99 would hardly be considered an "ideal" pneumothorax although many such cases have healed in the past. Most workers today would re-expand that type and do another form of collapse. The use of the bronchoscope has also been omitted together with the information obtained by its use. Finally, it doesn't seem to be unreasonable to expect that a book published in 1948 on tuberculosis would go into more detail on streptomycin treatment of tuberculosis and its complications.

Most of these points raised perhaps appear, and many probably are, out of proportion to their importance. They are nevertheless objections that most workers today will agree with. In this "smoke screen," however, the sterling worth of the chapters on phthisiogenesis; physical diagnosis; childhood tuberculosis; classical treatment; and other gems throughout the text should not be lost sight of. The illustrations are generally well chosen and of excellent quality. The binding and paper are of the best.

No one today in chest disease work can afford to be without this most valuable contribution to tuberculosis literature.

MEETING ON ANTHRACOSILICOSIS

The members of the College in West Virginia presented a program on "Anthracosilicosis" at the Daniel Boone Hotel, Charleston, on May 19. The speakers were Drs. Burgess Gordon, Peter A. Theodos, Hurley L. Motley and Leonard P. Lang, all members of the staff of the Jefferson Medical College Hospital, Philadelphia, who have been making a study of anthracosilicosis, especially among anthracite miners.

BRITISH TUBERCULOSIS ASSOCIATION MEETING

Dr. William Odgen, Regent of the College for Canada, addressed the British Tuberculosis Association at its annual conference held in Cambridge from April 6th to April 9th of this year. The title of his paper was "Twenty Years Observation on the Development of Pre-Clinical and Clinical Tuberculosis." His presentation was based on clinical material published as a symposium in "Diseases of the Chest" in July-August 1946, under the title "Foreseeing and Forestalling Tuberculosis."

It is interesting to note that three other Fellows made important contributions to the British Tuberculosis Association program, Dr. Irving Sarot of New York on resection for pulmonary tuberculosis with special reference to extrapleural resections and pleurectomy; Dr. J. M. Lemoine, of Paris on atelectasis and Dr. R. R. Trail who welcomed the Association and its guests to Papworth Village Settlement.

Dr. Joseph Lee of Hamilton, who is in England on an exchange arrangement, sponsored by the British National Association for the Prevention of Tuberculosis and who is attached to Clare Hall Sanatorium, Middlesex, also attended the meeting.

It might be added that all five Fellows of the College were able to meet informally at the University Arms, Cambridge, and indulge in a pleasant discussion of certain matters of mutual interest.

NEW OFFICERS OF AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION

At the annual meeting of the American Broncho-Esophagological Association, held in Chicago, Illinois, on April 18 and 19, the following officers were elected:

LeRoy A. Schall, M.D., Boston, Massachusetts, President
Edwin N. Broyles, M.D., Baltimore, Maryland, Secretary.

Obituaries

BURTON W. RHUBERRY
1914-1948

Dr. Burton W. Rhuberry was born on May 2, 1914 in Detroit, Michigan. He was a graduate of the American High School, Buenos Aires, Argentina, and received his medical degree from Northwestern University. His internship was served at Grace Hospital, Detroit, and he later became resident in thoracic surgery at the Detroit Tuberculosis Sanatorium. At the time of Dr. Rhuberry's death he was resident physician at the Leland Sanatorium. He was a Fellow of the American College of Chest Physicians, a member of the Wayne County Medical Society, the Michigan State Medical Society, the American Medical Association, the Phi Chi Fraternity and the Kismet Lodge FM. He is survived by his wife Dorothea and his daughter Gail Ann.

Willard B. Howes, M.D., Governor for Michigan.

ROBERT OSGOOD BROWN
1890-1949

The untimely death of Robert Osgood Brown, M.D., F.C.C.P., on February 1, 1949, is a tragic loss to his professional colleagues and his many friends.

Dr. Brown was born February 13, 1890 in Chicago, Illinois. He received his B.S. degree from the University of Chicago in 1912 and was graduated from Rush Medical College in June, 1914, interning at Cook County Hospital, Chicago until June, 1916. He was an officer in the National Guard and served with the Pershing Expedition on the Mexican Border in 1916. He entered the practice of medicine in Santa Fe, New Mexico in 1916, specializing in internal medicine and diseases of the chest.

He was a Fellow of the American College of Chest Physicians, serving as Governor for New Mexico since 1946. He was also a Fellow of the A.M.A. and of the American College of Physicians, a member of the American Heart Association, American Trudeau Society and the New Mexico Clinical Society.

Dr. Brown was prominent in New Mexico both in medical and in civic affairs. He was formerly Associate Medical Director of Sunmount Sanatorium, staff member of St. Vincent Sanatorium and Hospital; founder and member of the Board of Directors of The Santa Fe Clinic and Foundation for Research and Treatment of Cancer, Santa Fe. He was actively interested in Public Health and Welfare work in New Mexico, having served as Chairman of the New Mexico Public Welfare Board, Medical Consultant to the New Mexico Department of Public Welfare, and served for years as Chairman of the Legislative Committee of the State Medical Society. He was Past President of the New Mexico Medical Society, the New Mexico Tuberculosis Association, and was President of the Santa Fe County Tuberculosis Association at the time of his death.

He enjoyed an extensive and active practice. The community, his patients and his host of medical friends throughout the Southwest mourn his untimely death. We have lost a great and good friend and Doctor.

Carl H. Gellenthien, M.D., Regent.

DISEASES OF THE CHEST

AUTHOR INDEX

Volume XV, January - June, 1949

Aaron, A. H. and Leon J. Leahy. The Significance of Pleural Effusions as Indicating the Presence of Abdominal Disease 30

Acevedo, Rodolfo E. Cucchiani. Sociedad Argentina de Tisiologia. Report of Study 111

Adams, W. E. Differential Diagnosis and Treatment of Congenital Cystic Malformation of the Lung 60

Anderson, C. W., J. N. Medefind and J. D. Davis. Nutrition in Far Advanced Tuberculosis 734

Anderson, W. A. D. Pathologic Aspects of Atypical Pneumonias 337

Anido, H. and A. Rodriguez Diaz. Tetralogy of Fallot: Surgical Treatment 684

Armen, Robert N. and Thomas V. Frank. Electrocardiographic Patterns in Pneumothorax 709

Bailey, Charles P. The Surgical Treatment of Mitral Stenosis (Mitral Commissurotomy). Discussions by Evarts Graham, Gordon Murray and Horace G. Smithy 377

Bassin, Sydney. See Edlin, James S. et al 507

Bohorfoush, J. C. See Friedman, Louis L. et al 306

Boyden, Edward A. A Synthesis of the Prevailing Patterns of the Bronchopulmonary Segments in the Light of Their Variations .. 657

Brantigan, O. C. Cystic Disease of the Lung. Discussions by L. M. Serra and William A. Hudson 192

Briggs, John Francis and A. Karstens. Syphilitic Heart Disease 168

Bryson, William J. Propagating Pulmonary Artery Thrombosis (A Specific Syndrome) 366

deBustamante, O. Suarez. See Fariñas, Pedro L. et al 546

Carabelli, A. Albert. A New Mirror-Cannula for Laryngo-tracheo-bronchial Anesthesia, Medication, or Instillation of Opaque Oils 107

Laryngo - tracheo - bronchial Anesthesia for Bronchoscopy and Bronchography with Pontocaine 532

Carr, Duane, Edward F. Skinner, William E. Denman and Charles R. Kessler. Bronchography 92

Chortis, Panayiotis. A Case of Aspergillosis of the Lung 222

Clagett, O. T. Surgical Treatment of Emphysematous Blebs and Bullae. Discussions by Francis Woods, O. E. Egbert and Richard Meade 669

Cohen, Archibald C. Tuberculosis and Carcinoma of the Lung 607

Coleman, Jules V. See Hurst, Allan et al 581

Conway, James P. See Koszalka, Michael F. et al 591

Cromwell, Henry A. and G. N. Papanicolaou. Diagnosis of Cancer of the Lung by the Cytologic Method. Discussions by L. H. Clerf and S. M. Farber 412

Dack, Simon, Jacob Stone, David H. Paley and Arthur M. Master. Pulmonary Embolism: A Precipitating Factor of Acute Coronary Insufficiency. Discussion by Arthur E. Lamb 72

Davenport, L. Orton. See Friedman, Louis L. et al 306

Davis, J. D. See Anderson, C. W. et al 734

Denman, William E. See Carr, Duane et al 92

Dickman, Roy W. One Half Gram of Streptomycin in the Treatment of Pulmonary and Extrapulmonary Tuberculosis 422

Edlin, James S., Sydney Bassin and Samuel A. Thompson. Undergraduate and Postgraduate Teaching in Diseases of the Chest 507

Epstein, Issac. Mediastinal Defect with Interpleural Communication Observed During Pneumothorax Therapy 186

Platybasia Associated with an Unusual Case of Pulmonary Tuberculosis 563

Fariñas, Pedro L., O. Suarez de Bustamante, Luis M. Lott and Rene Revuelta. Intratracheal Atomization in the Treatment of Infectious Diseases of the Respiratory System 546

Feld, David D. and Valentine O'Malley. Bronchogenic Carcinoma 450

Ferguson, Lewis H. and William A. Werner. Cervical Vagus—Sympathetic Block in Pulmonary Embolism 741

Fidler, Alan and Abraham Melamed. Routine Fluororoentgen Chest Examinations of Hospital Admissions 346

Frank, Thomas V. and Robert N. Armen. Electrocardiographic Patterns in Pneumothorax 709

Friedman, Louis L., L. Orton Davenport and Joseph C. Bohorfoush. Extrapleural Pneumothorax. Discussion by Papken S. Mugrditchian 306

Fruin, Comdr. Richard L. The Pathogenesis of Primary Atypical Pneumonia 24

Gelenger, Stephen M. and Russell F. Wiggers. Relationship of the Pleural Fluid Sugar to Pulmonary Tuberculosis 325

Gines, Angel R., Eduardo Gould and J. A. Coronel Vera. An Appraisal of the Results of a Six-Year Tuberculin and Mass X-ray Survey of the Population of Asuncion 142

Gould, Eduardo. See Gines, Angel R. et al 142

Greer, Alvis E. Chronic Nontuberculous Pulmonary Infections and Their Sequelae 270

Habeeb, William J. Cavity Closure Following the Discontinuation of Ineffective Pneumothorax 97

Hayes, Edward W. Abstract of Replies to a Questionnaire on Intrapleural Artificial Pneumothorax 720

Hobby, A. Worth. Pulmonary Mycoses 174

Hoffman, Stanley H. and George A. Hyman. The Combined Use of Streptomycin and Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis 354

Holinger, Paul H. Editorial. Fifteenth Annual Meeting, American College of Chest Physicians 487

Hornbein, Ruth. See Hurst, Allan et al 581

Hughes, James R. See Volini, Italo F. et al 255

Humphrey, Arthur A. and Edwin G. Olmstead. Lipoid Pneumonia in Neuropsychiatric and Debilitated Patients 471

Hurst, Allan, Jules V. Coleman and Ruth Hornbein. The Place of Psychiatry in the Program of a Tuberculosis Hospital. Discussions by W. C. Voorsanger and F. Alexander 581

Hyman, George A. and Stanley H. Hoffman. The Combined Use of Streptomycin and Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis 354

Karstens, A. and J. F. Briggs. Syphilitic Heart Disease 168

Kessler, Charles R. See Carr, Duane et al 92

Knoepp, Louis F. The Importance of Various Mechanical and Circulatory Postoperative Pulmonary Complications *690*

Kornbluth, Alfred W. and F. Paul O'Hara. Thrombosis of the Main Stem of the Pulmonary Artery Associated with Pulmonary Tuberculosis 556

Koszalka, Michael F., Forrester Raine, James P. Conway and Mischa J. Lustok. Thoraco-Hepatic Amebiasis 591

Leahy, Leon J. and A. H. Aaron. The Significance of Pleural Effusions as Indicating the Presence of Abdominal Disease 30

Lees, H. D. Tuberculosis Among Medical and Academic Students .. 568

Logan, George B. The Diagnosis and Treatment of Acute Laryngotracheobronchitis 85

Lott, Luis M. See Fariñas, Pedro L. et al 546

Lustok, Mischa J. See Koszalka, Michael F. et al 591

Maclennan, M. Florence. Technique of Caulfeild's Inhibitive Test also of Tuberculo-Complement Fixation Test 517

Mantz, Herbert L. The Importance of Continued Studies in Tuberculosis 398

Marengo, J. Tanca and Julio Mata Martinez. Atelectasis of the Right Upper Lobe 226

Margulies, Bernard. Streptomycin in Tuberculosis of the Larynx 432

Martinez, Julio Mata and J. Tanca Marengo. Atelectasis of the Right Upper Lobe 226

Master, Arthur M. See Dack, Simon et al 72

Matthews, James H. and Walter L. Nalls. Idiopathic Spontaneous Hemopneumothorax 612

McDonald, John R. See Moersch, Herman J. et al 125

McGovern, Bernard E. The Problem of Bronchiectasis 208

Medefind, J. N. See Anderson, C. W. et al 734

Melamed, Abraham and Alan Fidler. Routine Fluororoentgen Chest Examinations of Hospital Admissions 346

Moersch, Herman J., L. A. Weed and John R. McDonald. Bacteriologic Examination of Tissues Surgically Removed as an Aid in the Diagnosis of Diseases of the Chest. Discussions by H. E. Johnson and S. M. Farber 125

Molinari, Leopoldo. Tuberculous Infection in the Children of Lima, Peru 40

Morgenstern, Philip. Pleural Fibrin Body Simulating Cardiac Aneurysm 103

Moyer, Ralph E. Pneumoperitoneum and Phreniclasia in the Treatment of Pulmonary Tuberculosis. Discussions by L. H. Hirsh and J. J. Mendelsohn 43

Myers, J. A. Editorial. Diseases of the Chest Now Published Monthly 113

Nalls, Walter L. and James H. Matthews. Idiopathic Spontaneous Hemopneumothorax 612

O'Hara, F. Paul and Alfred W. Kornbluth. Thrombosis of the Main Stem of the Pulmonary Artery Associated with Pulmonary Tuberculosis 556

Olmstead, Edwin G. and Arthur A. Humphrey. Lipoid Pneumonia in Neuropsychiatric and Debilitated Patients 471

Ornstein, George G. The Measurement of the Function of the Lungs. Discussions by B. P. Potter, A. L. Barach, E. R. Levine, G. G. Ornstein and G. E. Wright 280

Overholt, Richard H. and Beatty H. Ramsay. Editorial. Discretion in the Use of Bronchography 745

Painter, Samuel L. Tuberculosis in Children 329

Paley, David H. See Dack, Simon et al 72

Papanicolaou, George N. and Henry A. Cromwell. Diagnosis of Cancer of the Lung by the Cytologic Method. Discussions by L. H. Clerf and S. M. Farber 412

Peffer, J. R. See Volini, Italo F. et al 255

Poppe, J. K. Treatment of Aortic Aneurysms by Wrapping with Foreign Body. Discussions by Osler Abbott and J. E. Dailey 726

Potter, B. P. Aerosol Antibiotic Therapy in Suppurative Diseases of the Lung and Bronchi. Discussion by P. K. Bornstein 436

Raine, Forrester. See Koszalka, Michael F. et al 591

Rames, Eugene D. Early Diagnosis as the Means of Tuberculosis Control 404

Ramsay, B. H. and R. H. Overholt. Editorial. Discretion in the Use of Bronchography 745

Revuelta, Rene. See Fariñas, Pedro L. et al 546

Rodriguez Diaz, A. and H. Anido. Tetralogy of Fallot: Surgical Treatment 684

Rothstein, Emil. Benign Pleural Effusion and Ascites Associated with Adenocarcinoma of the Body of the Pancreas 603

Salkin, David. Postmortem Pneumothorax 1

Shamaskin, Arnold. Comments on Bacterial Resistance to Streptomycin 303

Skinner, Edward F. See Carr, Duane et al 92

Sodeman, W. A. Bagasse Disease of the Lungs. Discussion by A. S. Anderson 162

Stone, Jacob. See Dack, Simon et al 72

Sweany, Henry C. The Value of Streptomycin in the Treatment of Tuberculosis 631

Thompson, John V. Mediastinal Tumors and Cysts 480

Thompson, Samuel A. See Edlin, James S. et al 507

Vera, J. A. Coronel. See Gines, Angel R. et al 142

Viswanathan, Lt. Col. R. Pathogenesis of Pulmonary Atelectasis 460

Volini, Italo F., James R. Hughes and J. R. Peffer. A Comparative Study of Sulfadiazine, Penicillin, and Penicillin Combined with Sulfadiazine in the Treatment of Lobar Pneumonia. Discussions by H. F. Dowling and I. F. Volini 255

Weed, L. A. See Moersch, Herman J. et al 125

Werner, William A. and Lewis H. Ferguson. Cervical Vagus—Sympathetic Block in Pulmonary Embolism 741

Wiggers, Russell F. and Stephen M. Gelenger. Relationship of the Pleural Fluid Sugar to Pulmonary Tuberculosis 325

DISEASES OF THE CHEST

SUBJECT INDEX

Volume XV, January - June, 1949

Abdominal Disease and Pleural Effusion 30
Adenocarcinoma of Pancreas 603
Aerosol, Antibiotic 436
Amebiasis, Thoraco-hepatic 591
Anesthesia, Bronchoscopy and Bronchography 532
Anesthesia, Mirror-Cannula for 107
Aneurysms, Aortic. Treatment of 726
Aspergillosis of the Lung 222
Asuncion: Tuberculin and X-ray Survey 142
Atelectasis 226, 460
Atomization, Intratracheal 546
Bacteriologic Examination of Tissues Surgically Removed 125
Bagasse Disease 162
Blebs and Bullae. Surgical Treatment of 669
Book Reviews:
- Zinsser's Textbook of Bacteriology. By David Smith and Donald S. Martin et al 122
- A Practical Manual of Diseases of the Chest. By Maurice Davidson 123
- Tuberculosis (A Discussion of Phthisiogenesis, Immunology, Pathologic Physiology, Diagnosis and Treatment). By Francis Marion Pottenger 751
- The Chest and the Heart. By J. Arthur Myers and C. A. McKinlay 750

Bronchiectasis 208
Bronchography 92, 745
Bronchopulmonary Segments. Synthesis of Prevailing Patterns 657
By-Laws of American College of Chest Physicians 233
Cancer of the Lung. Diagnosis of 412
Carcinoma and Tuberculosis of the Lung 607
Carcinoma, Bronchogenic 450
Cavity Closure 97
Children and Tuberculosis 329
Coronary Insufficiency 72
Cystic Disease of the Lung 192
Cystic Malformation of the Lung 60
Diseases of the Chest Published Monthly 113
Electrocardiographic Patterns in Pneumothorax 709
Embolism, Pulmonary 72, 741
Emphysematous Blebs and Bullae 669
Extrapleural Pneumothorax 306

Fibrin Body 103
Heart Disease, Syphilitic 168
Hemopneumothorax, Spontaneous 612
Hospital Admissions—Examinations 346
Infections, Nontuberculous, Pulmonary 270
Laryngo-tracheo-bronchial Anesthesia 107
Laryngotracheobronchitis 85
Lima, Peru. Tuberculous Infection 40
Lung, Cystic Malformation 60
Lungs, Measurement of Function 280
Mediastinal Defect 186
Mediastinal Tumors and Cysts 480
Meetings:
Fifteenth Annual, American College of Chest Physicians 487
VIII Congreso Panamericano de Tuberculosis (ULAST), III Congreso Nacional de Tuberculosis y Silicosis 493
IX Congreso Panamericano del Niños 624
Mirror Cannula, New 107
Mitral Stenosis, Surgical Treatment 377
Mycosis, Pulmonary 174
Nerve Block, Cervical Vagus and Sympathetic 741
Nutrition in Advanced Tuberculosis 734
Obituaries:
Ameuille, Pierre 124
Anglin, George Chambers 506
Brown, Robert Osgood 754
Fox, Irvin Reginals 506
Rhuberry, Burton W. 754
Pancreas, Pleural Effusion and Ascites 603
Penicillin and Sulfadiazine in Lobar Pneumonia 255
Phreniclasia 43
Platybasia with Pulmonary Tuberculosis 563
Pleural Effusion in Abdominal Disease 30
Pleural Fibrin Body Simulating Cardiac Aneurysm 103
Pleural Fluid Sugar and Tuberculosis 325
Pneumonia:
Atypical 337
Lipoid 471
Lobar 255
Primary Atypical 24
Pneumoperitoneum and Phreniclasia in Pulmonary Tuberculosis 43
Pneumoperitoneum and Streptomycin in Pulmonary Tuberculosis 354
Pneumothorax:
Electrocardiographic Patterns 709
Extrapleural 306
Ineffective 97
Intrapleural Artificial 720

Mediastinal Defect 186
Postmortem 1
Postgraduate Course in Diseases of the Chest, Philadelphia 627
Postgraduate Teaching 507
Postmortem Pneumothorax 1
Psychiatry in Tuberculosis Hospitals 581
Pulmonary Artery, Thrombosis of 556
Pulmonary Complications, Postoperative; Mechanical and Circulatory 690
Pulmonary Mycoses 174
Silicosis, Congress on 493
Streptomycin:
And Pneumoperitoneum in Pulmonary Tuberculosis 354
Bacterial Resistance to 303
In Laryngeal Tuberculosis 432
In Pulmonary and Extrapulmonary Tuberculosis 422
In Treatment of Tuberculosis 631
Study 111
Students and Tuberculosis 568
Sulfadiazine and Penicillin in Treatment of Lobar Pneumonia 255
Suppurative Disease, Antibiotic Therapy 436
Syphilitic Heart Disease 168
Test, Caulfeild's Inhibitive, Tuberculo-Complement Fixation 517
Tetralogy of Fallot: Surgical Treatment 684
Thrombosis, Pulmonary Artery 366, 556
Tissues, Bacteriologic Examination 125
Tuberculosis:
Among Students 568
And Carcinoma of Lung 607
In Children 329
Continued Studies in 398
Control. Early Diagnosis 404
Minimal 485
Tuberculous Infection in Lima, Peru 40
Tumors, Mediastinal 480

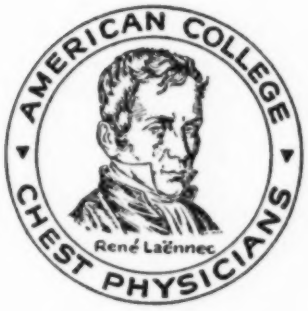
VOLUME XV NUMBER 6

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



PUBLISHED MONTHLY

JUNE
1949

EXECUTIVE OFFICE, 500 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS
PUBLICATION OFFICE, ALAMOGORDO ROAD, EL PASO, TEXAS

Entered as Second Class Matter August 18, 1936, at the Postoffice at El Paso, Texas
Under the Act of Congress of August 12, 1912.